No. 01-344-CFX
Status: GRANTED

Title: Tommy G. Thompson, Secretary of Health and Human Services, et al., Petitioners
v.
Western States Medical Center, et al.

Docketed:
August 27, 2001

Court: United States Court of Appeals for the Ninth Circuit

Counsel for petitioner: Solicitor General

Counsel for respondent: Reiter,Michael A., Lionel,Samuel S., Labson,Michael S., Hoffman,Howard M.

Entry	Date	Note	Proceedings and Orders
1	Jul 13 2001	G	Application (01A49) to extend the time to file a petition for a writ of certiorari from July 26, 2001 to August 25, 2001, submitted to Justice O'Connor.
2	Jul 15 2001		Application (01A49) granted by Justice O'Connor extending the time to file until August 25, 2001.
3	Aug 24 2001	G	Petition for writ of certiorari filed. (Response due September 26, 2001)
4	Sep 25 2001		Brief of respondents Western States Medical Center, et al. in opposition filed.
5	Oct 9 2001		Reply brief of petitioners Tommy G. Thompson, Secretary of H&HS, et al. filed.
6	Oct 10 2001		DISTRIBUTED. October 26, 2001 (Page 16)
7	Oct 29 2001		Petition GRANTED. SET FOR ARGUMENT February 26, 2002. **********
8	Dec 11 2001	G	Motion of the Solicitor General to dispense with printing the joint appendix filed.
9	Dec 13 2001		Brief of petitioners Tommy G. Thompson, Secretary of H&HS, et al. filed.
10	Dec 21 2001		CIRCULATED.
11	Jan 7 2002		Motion of the Solicitor General to dispense with printing the joint appendix GRANTED.
13	Jan 9 2002	X	Brief amicus curiae of American Pharmaceutical Association filed.
12	Jan 11 2002	X	Brief amici curiae of Julian Whitaker, et al. filed.
14	Jan 17 2002	X	Brief amicus curiae of International Academy of Compounding Pharmacists filed.
15	Jan 17 2002	X	Brief of respondents Western States Medical Center, et al. filed.
16	Jan 17 2002	X	Brief amicus curiae of National Community Pharmacists Association filed.
17	Feb 19 2002	X	Reply brief of petitioner Tommy G. Thompson, Secretary of H&HS, et al. filed.
18	Feb 26 2002		ARGUED.

Supreme Court, U.S.
FILED
01 344 AUG 2 4 2001
OFFICE OF THE CLERK

No.

In the Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

THEODORE B. OLSON
Solicitor General
Counsel of Record

STUART E. SCHIFFER
Acting Assistant Attorney General

EDWIN S. KNEEDLER
Deputy Solicitor General

MATTHEW D. ROBERTS
Assistant to the Solicitor General

DOUGLAS N. LETTER
Attorney

Department of Justice
Washington, D.C. 20530-0001
(202) 514-2217

QUESTION PRESENTED

In the Food and Drug Administration Modernization Act of 1997 (FDAMA), Congress enacted a limited exemption from the new drug approval (and certain other) requirements of the Federal Food, Drug, and Cosmetic Act, for drugs compounded by pharmacists. See 21 U.S.C. 353a. The question presented is whether FDAMA's limitation of that exemption to pharmacists who do not solicit prescriptions for or advertise specific compounded drugs is consistent with the First Amendment.

PARTIES TO THE PROCEEDINGS

Petitioners are Tommy G. Thompson, Secretary of Health and Human Services, and Bernard A. Schwetz, Acting Principal Deputy Commissioner, United States Food and Drug Administration. Respondents are Western States Medical Center, Women's International Pharmacy, Health Pharmacy, Apothecure, College Pharmacy, Lakeside Pharmacy, and Wedgewood Village Pharmacy.

TABLE OF CONTENTS

	Page
Opinions below	1
Jurisdiction	2
Constitutional and statutory provisions involved	2
Statement	2
Reasons for granting the petition	11
Conclusion	26
Appendix A	1a
Appendix B	16a
Appendix C	60a
Appendix D	71a
Appendix E	78a
Appendix F	80a

TABLE OF AUTHORITIES

Cases:

Board of Trustees v. *Fox*, 492 U.S. 469 (1989)	24
Cedars North Towers Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978)	4-5
Central Hudson Gas & Elec. Corp. v. *Public Serv. Comm'n*, 447 U.S. 557 (1980)	7-8
Florida Bar v. *Went For It, Inc.*, 515 U.S. 618 (1995)	17, 24
Greater New Orleans Broad. Ass'n v. *United States*, 527 U.S. 173 (1999)	9, 22
Lorillard Tobacco Co. v. *Reilly*, 121 S. Ct. 2404 (2001)	17, 24
Professionals & Patients for Customized Care v. *Shalala*, 847 F. Supp. 1359 (S.D. Tex. 1994), aff'd, 56 F.3d 592 (5th Cir. 1995)	3, 4, 15
Rubin v. *Coors Brewing Co.*, 514 U.S. 476 (1995)	9
United States v. *Edge Broad. Co.*, 509 U.S. 418 (1993)	16, 19
United States v. *Gainey*, 380 U.S. 63 (1965)	11, 25

Cases—Continued: Page

United States v. *Rutherford*, 442 U.S. 544 (1979) 11-12, 17
United States v. *Sene X*, 479 F. Supp. 970 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983) 4
Warner-Lambert Co. v. *Heckler*, 787 F.2d 147 (3d Cir. 1986) 12, 17, 20
Weinberger v. *Hynson, Westcott & Dunning*, 412 U.S. 609 (1973) 3, 12, 15, 17, 20, 24

Constitution and statutes:

U.S. Const. Amend. I 2, 7, 8, 10, 11, 25
Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 ..... 4, 11
21 U.S.C. 353a (Supp. V 1999) ..... *passim*
21 U.S.C. 353a(a) (Supp. V 1999) ..... *passim*
21 U.S.C. 353a(a)(1) (Supp. V 1999) 6
21 U.S.C. 353a(b)(1) (Supp. V 1999) 9
21 U.S.C. 353a(b)(1)(A) (Supp. V 1999) 6, 21
21 U.S.C. 353a(b)(1)(B) (Supp. V 1999) 6, 21
21 U.S.C. 353a(b)(1)(C) (Supp. V 1999) 6
21 U.S.C. 353a(b)(1)(D) (Supp. V 1999) 6, 9, 21
21 U.S.C. 353a(b)(2) (Supp. V 1999) 6
21 U.S.C. 353a(b)(3) (Supp. V 1999) 10, 21, 22, 23
21 U.S.C. 353a(b)(3)(A) (Supp. V 1999) 6
21 U.S.C. 353a(b)(3)(B) (Supp. V 1999) 6
21 U.S.C. 353a(c) (Supp. V 1999) 7, 8, 11, 21, 23, 24, 25
Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.* 2, 11
21 U.S.C. 321(p) 2, 4, 12
21 U.S.C. 331 (1994 & Supp. V 1999) 3
21 U.S.C. 331(d) 2, 12
21 U.S.C. 351 (1994 & Supp. V 1999) 3
21 U.S.C. 352 (1994 & Supp. V 1999) 3

Statutes—Continued: Page

21 U.S.C. 355(a) 2, 12
21 U.S.C. 355(b) (1994 & Supp. V 1999) 2-3
21 U.S.C. 360 3
21 U.S.C. 360(g)(1) 3, 15
21 U.S.C. 360(h) 3
21 U.S.C. 360(j) 3
21 U.S.C. 374(a)(2) 15
21 U.S.C. 374(a)(2)(A) 3

Miscellaneous:

143 Cong. Rec.:
p. S9839 (daily ed. Sept. 24, 1997) 5, 14, 15, 19
p. S12,242 (daily ed. Nov. 5, 1997) 23
FDA Reform Legislation: Hearings Before the Subcomm. on Health and the Env't of the House Comm. on Commerce, 104th Cong., 2d Sess. (1996) 13, 14, 18
H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. (1997) 5, 13, 14, 18
S. Rep. No. 43, 105th Cong., 1st Sess. (1997) ... 5, 13, 14, 18, 19

In the Supreme Court of the United States

No.

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

PETITION FOR A WRIT OF CERTIORARI

The Solicitor General, on behalf of the Secretary of Health and Human Services and the Acting Principal Deputy Commissioner of the Food and Drug Administration, respectfully petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Ninth Circuit in this case.

OPINIONS BELOW

The opinion of the court of appeals (App., *infra*, 1a-15a) is reported at 238 F.3d 1090. The opinion of the district court (App., *infra*, 16a-59a) is reported at 69 F. Supp. 2d 1288. An earlier opinion of the district court granting respondents' motion for a temporary restraining order (App., *infra*, 60a-70a) is unreported.

JURISDICTION

The judgment of the court of appeals was entered on February 6, 2001. A petition for rehearing was denied on April 27, 2001 (App., *infra*, 78a-79a). On July 15, 2001, Justice O'Connor extended the time within which to file a petition for a writ of certiorari to and including August 25, 2001. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

CONSTITUTIONAL AND STATUTORY PROVISIONS INVOLVED

The First Amendment to the United States Constitution provides that "Congress shall make no law * * * abridging the freedom of speech, or of the press." The pertinent provisions of the Food and Drug Administration Modernization Act of 1997, 21 U.S.C. 353a (Supp. V 1999), and the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.* (1994 & Supp. V 1999), are reprinted in an appendix to this petition. App., *infra*, 80a-107a.

STATEMENT

1. a. The Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.* (1994 & Supp. V 1999), defines a "new drug" as "[a]ny drug * * * not generally recognized * * * as safe and effective for use under the conditions prescribed." 21 U.S.C. 321(p). The FDCA generally requires that, before a new drug may be introduced into interstate commerce, the manufacturer or distributor obtain the approval of the Food and Drug Administration (FDA). See 21 U.S.C. 355(a), 331(d). In order to obtain that approval, the manufacturer or distributor must demonstrate to the FDA's satisfaction that the drug is both safe and effective for each intended use. See 21 U.S.C. 355(b) (1994 & Supp. V 1999); *Weinberger* v. *Hynson, Westcott & Dunning*, 412 U.S. 609, 613, 629, 632 (1973).

The FDCA also imposes standards for the manufacturing and labeling of drugs in order to ensure that manufacturing processes and drug ingredients are safe and effective and that consumers and physicians have adequate information about drug contents and effects. See 21 U.S.C. 351, 352 (1994 & Supp. V 1999). The FDCA prohibits the sale and distribution of "adulterated" or "misbranded" drugs. See 21 U.S.C. 331 (1994 & Supp. V 1999).

In addition, to facilitate regulatory oversight, the FDCA imposes registration, inspection, and reporting requirements on drug manufacturers. See 21 U.S.C. 360 (requiring domestic drug manufacturers to register with the Secretary); 21 U.S.C. 360(h) (requiring inspection of drug manufacturers at least once every two years); 21 U.S.C. 360(j) (requiring each registered drug manufacturer to "file with the Secretary a list of all drugs" that it manufactures for commercial distribution). The FDCA contains a limited exemption from its registration and some of its inspection requirements, however, for pharmacies that comply with state regulations and that do not "manufacture" or "compound" drugs other than in "the regular course of their business of dispensing or selling drugs * * * at retail." 21 U.S.C. 360(g)(1), 374(a)(2)(A).

b. Compounding is a process by which a pharmacist "combines, mixes, or alters ingredients to create a certain medication for a patient." *Professionals & Patients for Customized Care* v. *Shalala*, 847 F. Supp. 1359, 1361 (S.D. Tex. 1994), aff'd, 56 F.3d 592 (5th Cir. 1995). The process encompasses a range of pharmacy activities, including the modification of approved drugs "to provide medications that are not commercially

available, such as diluted dosages for children, or to alter the form of a medication for easier consumption." *Id.* at 1361.

When a pharmacy compounds a drug, the pharmacy creates a "new drug" because the compounded product is not generally recognized as safe and effective. See 21 U.S.C. 321(p). For that reason, interstate distribution of compounded drug products without compliance with the FDCA's approval requirements for new drugs was unlawful before enactment of the Food and Drug Administration Modernization Act of 1997 (FDAMA), Pub. L. No. 105-115, 111 Stat. 2296. See *Professionals & Patients*, 56 F.3d at 593 n.3; App., *infra*, 72a (1992 FDA Compliance Policy Guide). Nonetheless, the FDA recognized that compounding in response to a valid prescription in order to meet the medical needs of an individual patient for whom commercially available drugs are inadequate may serve an important public purpose for which the health benefits outweigh the risks. Therefore, "the FDA as a matter of policy [did] not historically [bring] enforcement actions against pharmacies engaged in traditional compounding." 56 F.3d at 593 n.3.

The FDA did take action, however, when compounding was outside the scope of normal pharmacy practice and compounded drugs were mass-produced and distributed in a manner tantamount to the manufacture of unapproved new drugs. See App., *infra*, 73a-74a. The FDA issued warning letters, see *id.* at 73a, and sometimes brought judicial enforcement actions against pharmacies engaged in drug manufacturing under the guise of compounding. *E.g.*, *United States* v. *Sene X*, 479 F. Supp. 970, 978 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983); *Cedars North Towers*

Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,828 (S.D. Fla. Aug. 28, 1978). Among the factors that the FDA considered in determining whether a pharmacy was manufacturing drugs rather than engaging in traditional compounding were whether the pharmacy was "[s]oliciting business (e.g., promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products," or "[d]istributing inordinate amounts of compounded products out of state." App., *infra*, 76a-77a.

2. Congress addressed the compounding issue when it enacted FDAMA in 1997. The section of FDAMA at issue in this case, now codified at 21 U.S.C. 353a (Supp. V 1999), "bring[s] the legal status of compounding in line with FDA's longstanding enforcement policy of regulating only drug manufacturing, not ordinary pharmacy compounding." 143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997) (Sen. Kennedy). Section 353a seeks to "ensure continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. 94 (1997) (Conf. Rep.); accord S. Rep. No. 43, 105th Cong., 1st Sess. 67 (1997) (S. Rep.).

Rather than leaving to the enforcement discretion of the FDA the determination of when compounding should be restricted, Congress chose to delineate in the FDCA itself certain limited circumstances under which pharmacy compounding would be exempt from requirements that apply to drug manufacturers. If certain conditions are met, Section 353a thus exempts compounded drug products from the FDCA's provisions governing

good manufacturing practices, adequate directions for use, and new drug approval. Under those conditions, which echo the FDA's pre-1997 practices regarding compounding, (1) the compounding must be performed by a licensed pharmacist or physician in response to a valid prescription made by a licensed practitioner, see 21 U.S.C. 353a(a)(1) (Supp. V 1999); (2) the compounding must use only ingredients that comply with various quality-control standards, see 21 U.S.C. 353a(b)(1)(A) and (B) (Supp. V 1999); (3) the compounded product may not be a drug product identified by regulation as presenting difficulties for compounding that would adversely affect safety or efficacy, see 21 U.S.C. 353a(b)(3)(A) (Supp. V 1999); (4) the compounding may not produce a drug that has been withdrawn from the market for safety reasons, see 21 U.S.C. 353a(b)(1)(C) (Supp. V 1999); and (5) the pharmacist may not compound regularly or in inordinate amounts any drug products that are essentially copies of a commercially available drug product, see 21 U.S.C. 353a(b)(1)(D), 353a(b)(2) (Supp. V 1999). FDAMA also limits the total volume of compounded drug products that a pharmacy may distribute out of State. See 21 U.S.C. 353a(b)(3)(B) (Supp. V 1999).

In addition, FDAMA makes the availability of the exemption of compounded drugs from certain FDCA requirements contingent upon the pharmacy's compliance with limitations on advertising and promotion of compounded drug products. Section 353a(a) exempts pharmacy compounding from the new drug approval and other requirements only if the compounded drug is produced "based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified

patient." 21 U.S.C. 353a(a) (Supp. V 1999). Section 353a(c) further provides that a pharmacy is entitled to the exemption only if it "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug." 21 U.S.C. 353a(c) (Supp. V 1999). The advertising limitation does not, however, prevent the pharmacy from advertising that it performs compounding services generally. 21 U.S.C. 353a(c) (Supp. V 1999).

3. In November 1998, shortly before the relevant provisions of FDAMA took effect, respondent pharmacies, which regularly compound drugs in significant quantities, commenced this suit in the United States District Court for the District of Nevada against the Secretary and the Commissioner of Food and Drugs. Respondents sought a declaratory judgment that Sections 353a(a) and (c) violate the First Amendment and an order enjoining enforcement of those provisions against them.

The district court initially granted respondents a temporary restraining order that enjoined the government from enforcing Section 353a(c). App., *infra*, 60a-70a. The parties subsequently filed cross-motions for summary judgment. The district court concluded that Sections 353a(a) and (c) violate the First Amendment, granted respondents' motion, denied the government's motion, and permanently enjoined the FDA from enforcing the solicitation and advertising restrictions in Sections 353a(a) and (c). App., *infra*, 16a-57a. The court further held that the restrictions are severable from the remainder of Section 353a. *Id.* at 58a-59a.

4. The United States Court of Appeals for the Ninth Circuit affirmed in part and reversed in part. App., *infra*, 1a-16a.

a. Applying the four-part test enunciated in *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557 (1980), for determining the constitutionality of restrictions on commercial speech, the court of appeals affirmed the district court's holding that Sections 353a(a) and (c) violate the First Amendment. App., *infra*, 4a-12a. Because the government did not contest that the advertising and solicitation limitations in Section 353a apply to lawful, non-misleading speech, the court of appeals began its analysis with the second element in the *Central Hudson* analysis—whether the governmental interests that underlie Section 353a's solicitation and advertising conditions are substantial. *Id.* at 5a.

The court of appeals recognized that the government has a substantial interest in "protecting the public health and safety" and in "preserving the integrity of the drug approval process." App., *infra*, 5a-6a. The court also recognized that "[t]he government's effort to balance competing goals can be a substantial interest." *Id.* at 6a. The court concluded, however, that the government had not demonstrated that "its interest in striking a balance between ensuring compounding availability and limiting widespread compounding is substantial." *Id.* at 7a. The court reached that conclusion because, in its view, "[t]here is insufficient evidence in the record to conclude that the government has a substantial interest in preventing widespread compounding." *Ibid.*

Turning to the third step in the *Central Hudson* analysis, the court further held that the solicitation and advertising limitations in Section 353a do not directly advance either of the asserted interests that the court did find to be substantial—protecting the public health and safety and preserving the integrity of the drug

approval process. App., *infra*, 7a-10a. The court reasoned that the government "has not offered evidence or arguments to explain sufficiently why such restrictions will reduce the type of consumption of compounded drugs that is harmful, and even admits that it has a substantial interest in ensuring the availability of compounded drugs." *Id.* at 7a-8a. The court also was of the view that, "[w]ithout the advertising restrictions, other safeguards exist to protect the public." *Id.* at 8a (citing 21 U.S.C. 353a(a) (Supp. V 1999) (requiring valid prescription for compounded drug products), 353a(b)(1) (Supp. V 1999) (limiting substances that pharmacists may use in compounded products), and 353a(b)(1)(D) (Supp. V 1999) (preventing pharmacists from regularly compounding drugs that are essentially copies of commercially available products)).

In addition, relying on *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476 (1995), and *Greater New Orleans Broadcasting Ass'n* v. *United States*, 527 U.S. 173 (1999), the court concluded that Section 353a "is so riddled with exceptions that it is unlikely that the speech restrictions would actually succeed in depressing the volume of compounded drugs." App., *infra*, 9a. The court observed that "pharmacists can advertise their compounding services and promote their skills at medical trade events so long as they do not promote the compounding of any *particular* drug," and that a pharmacist may call a physician and recommend a compounded drug if a patient comes in with a prescription for a commercial drug and provides information to the pharmacist that indicates that the patient might require a compounded product. *Ibid.* In addition, the court noted that FDAMA permits compounded drugs to constitute at least 5% of the total interstate distributions and 100% of the total intrastate distributions

by a particular pharmacy. *Ibid.* (citing 21 U.S.C. 353a(b)(3) (Supp. V 1999)).

The court next addressed the fourth *Central Hudson* factor and concluded that the advertising and solicitation restrictions "are more extensive than necessary to achieve the asserted government interest." App., *infra*, 10a. The court suggested that, instead of limiting advertising, the FDA could require disclaimers stating that the compounded drugs being advertised had not been subjected to the FDA's approval process. *Ibid.* The court also offered the alternative of requiring all compounded drugs, including those created on an individual basis as part of the traditional practice of pharmacy, to undergo the safety and effectiveness testing required for new drugs under the FDCA. *Ibid.* The court rejected the government's argument that those alternatives would not address the interest in drawing a workable distinction between traditional, patient-based compounding and manufacturing of new drugs, noting that it had already determined that the government's interest in balancing those competing goals is not substantial. *Id.* at 11a.

b. Although the court of appeals affirmed the district court's judgment insofar as it held that the solicitation and advertising provisions in Section 353a violate the First Amendment, the court, accepting the government's submission, reversed the district court's decision to sever those provisions from the rest of Section 353a. App., *infra*, 12a-15a. The court reasoned that "Congress intended to provide access to compounded drugs while preventing pharmacies from making an end run around the FDA's drug manufacturing requirements." *Id.* at 12a. Because "Congress meant to exempt compounding pharmacists from FDCA requirements only in return for a prohibition on

the promotion of specific compounded drugs," the court concluded that the solicitation and advertising restrictions could not be severed from the rest of Section 353a. *Id.* at 13a-14a. Accordingly, the court invalidated Section 353a in its entirety. *Id.* at 15a.

REASONS FOR GRANTING THE PETITION

The Food and Drug Administration Modernization Act of 1997 (FDAMA), 21 U.S.C. 353a (Supp. V 1999), provides a limited exemption from the new drug approval and certain other requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, for drugs compounded by pharmacists. The court of appeals has held unconstitutional under the First Amendment the solicitation and advertising limitations that Congress adopted as conditions on the availability of that new exemption. In striking down those carefully crafted provisions of the federal food and drug laws, the court unduly limited Congress's authority to regulate the interstate distribution of new drugs while at the same time accommodating individual needs for compounding of drugs, and thereby undermined the ability of the Food and Drug Administration (FDA) to preserve the regulatory framework for protecting the public health and safety. That mistaken "exercise of the grave power of annulling an Act of Congress" warrants this Court's review. See *United States* v. *Gainey*, 380 U.S. 63, 65 (1965).[1]

1. As both Congress and this Court have recognized, the widespread distribution of drugs that have not been

---

[1] We agree with the court of appeals' conclusion (App., *infra*, 12a-15a) that, if the solicitation and advertising provisions in Sections 353a(a) and (c) are unconstitutional, they are not severable from the other provisions of Section 353a. We therefore do not seek review of that holding in this Court.

shown to be safe and effective poses substantial health risks. See *United States* v. *Rutherford*, 442 U.S. 544, 556-557 (1979); *Weinberger* v. *Hynson, Westcott & Dunning*, 412 U.S. 609, 622 (1973). Congress enacted the FDCA to ensure that drugs are not introduced into interstate commerce unless they first have been determined to be safe and effective. Accordingly, at the heart of the FDCA is the requirement that the manufacturer or distributor of a new drug obtain approval for each of its intended uses from the FDA before distributing the drug in interstate commerce. See 21 U.S.C. 321(p), 331(d), 355(a). That requirement rests on two related premises: first, proof of safety and efficacy must be established by rigorous, scientifically valid studies rather than the clinical impressions of individual doctors, who cannot by themselves compile and master the necessary information; and, second, those who promote new drugs and realize profits from their distribution should bear the often substantial costs of the investigations necessary to establish safety and efficacy. See *Hynson, Westcott & Dunning*, 412 U.S. at 619, 629-630; *Warner-Lambert Co.* v. *Heckler*, 787 F.2d 147, 156 (3d Cir. 1986). The new drug approval requirements ensure that drug manufacturers have the incentive to undertake the studies necessary to demonstrate that the drugs they seek to market are in fact safe and effective. For these reasons, the new drug approval process is a critical component of the FDCA's regulatory framework for the protection of public health and safety.

Congress came to recognize, however, that compounding offers an important health benefit for individual patients who, for particularized medical reasons such as allergies, cannot use the versions of drugs that have been approved by the FDA and are commercially available. Because obtaining FDA approval is a costly process, requiring approval of all drug products compounded by pharmacies would, as a practical matter, eliminate the availability of compounded drugs for those individual patients who have no alternative treatment. See S. Rep. 67 (exemption from approval requirements needed to "ensure continued availability of compounded drug products as a component of individualized drug therapy"); Conf. Rep. 94 (same). Congress therefore enacted Section 353a, which provides an exemption from the new drug approval requirements for traditional pharmaceutical compounding.

At the same time, Congress understood that an unrestricted exemption for compounded drugs from the new drug approval requirements would seriously impair the integrity of the drug approval process. A pharmacy could mass produce a particular drug product, stimulate demand for the product through advertising, and thereby effectively manufacture and distribute the drug in interstate commerce without complying with the drug approval requirements, which are critical to protecting the public health and safety. See *FDA Reform Legislation: Hearings Before the Subcomm. on Health and the Env't of the House Comm. on Commerce*, 104th Cong., 2d Sess. 31, 125 (1996) (*Hearings*) (testimony of Hon. David A. Kessler, Commissioner, FDA); *id.* at 59 (FDA Analysis). Indeed, regulatory experience had shown that manufacturing under the guise of compounding was not a mere hypothetical threat, but an existing problem. See App., *infra*, 72a-74a; *Hearings* 120-121 (Kessler testimony).

Permitting manufacturing to occur under the guise of compounding would have serious consequences beyond the potential for drugs that are unsafe or ineffective to

enter the marketplace. It would strike at the core of the drug approval requirements, and thus at the core of the FDCA itself. If drug producers could mass produce drugs through a pharmacy engaged in widespread compounding, and thus bypass the approval process, manufacturers would have far less incentive to bear the cost of establishing that the drugs they seek to market are in fact safe and effective. See *Hearings* 31, 59.

Section 353a thus reflects a carefully balanced congressional effort to "ensure continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." Conf. Rep. 94; accord S. Rep. 67. Rather than rely (as it had in the past) on the FDA's exercise of enforcement discretion to strike that balance, Congress sought instead to "bring the *legal status* of compounding in line with FDA's longstanding enforcement policy." 143 Cong. Rec. at S9839 (Sen. Kennedy) (emphasis added); see S. Rep. 67 (FDAMA "establishes the parameters under which compounding is appropriate and lawful"). Building on the FDA's enforcement experience, Congress sought to draw a clear line to distinguish traditional, individualized compounding from compounding that is tantamount to manufacturing. See 143 Cong. Rec. at S9839 (Sen. Kennedy); *ibid.* (Sen. Hutchinson) (legislation "would exempt pharmacy compounding from several regulatory requirements but would not exempt drug manufacturing from the act's requirements").

As the FDA had previously determined based on its enforcement experience, see App., *infra*, 72a, 76a, Congress reasonably concluded that advertising of particular drug products is a business practice that distinguishes manufacturing from traditional pharmaceutical

compounding. Traditional compounding involves the provision of a service in response to a physician's prescription and an individual patient's special medical need. See 21 U.S.C. 360(g)(1), 374(a)(2); *Professionals & Patients*, 56 F.3d at 593; App., *infra*, 71a-72a. Drug manufacturing, in contrast, is the mass production of a drug product, typically for a substantial market. Promotion of the manufactured product to physicians or the public is thus a common feature of manufacturing, but not of traditional compounding on an individualized basis in response to the medical needs of particular patients. See *id.* at 72a. By confining the compounding exemption to pharmacies that do not engage in conduct that is characteristic of manufacturing, Congress ensured that "the exemption would not create a loophole that would allow unregulated drug manufacturing to occur under the guise of pharmacy compounding." 143 Cong. Rec. at S9839 (Sen. Kennedy).

Focusing on promotion of the compounded drug as a trigger for application of the regulatory approval process also reflects the important underlying premise of the FDCA that the public health is best served when those who develop and promote new drugs bear the cost of proving that those drugs are safe and effective. See *Hynson, Westcott & Dunning*, 412 U.S. at 619, 629-630. If compounders could actively promote their products through advertising without bearing those costs, they would enjoy an unfair advantage over traditional drug manufacturers, who must comply with the approval requirements. That unfair advantage would undermine the incentive of all drug manufacturers to comply with those requirements, which is the FDCA's central mechanism to ensure that drugs introduced into interstate commerce are safe and effective for their intended uses. Section 353a was drafted to accom-

modate these competing considerations while promoting the FDCA's overriding goal of protecting the public health and safety.

2. The court of appeals erred in striking down Congress' carefully crafted approach to compounding. The court's erroneous holding flowed from its threshold determination that one of the important interests asserted by the government is not substantial. As discussed above, in enacting Section 353a, Congress attempted to balance competing goals: (1) preserving the effectiveness and integrity of the new drug approval process and the protection of the general public that it provides, and (2) preserving the availability of compounded drugs for those individual patients who, for particularized medical reasons, cannot use commercially available products that have been approved by the FDA. The court of appeals erroneously failed to apprehend and refused to credit the substantiality of the government's interest in balancing those competing, but independently compelling, interests by carving out only a narrow exception to the drug approval process. That threshold error in turn led the court to the erroneous conclusion at step three of the *Central Hudson* analysis that Section 353a does not directly and materially advance the government's goals, and at step four of the *Central Hudson* analysis that Section 353a is not sufficiently tailored to achieve those goals.

a. The Ninth Circuit recognized that a "congressional policy of balancing [competing] interests [can be a] substantial government interest that satisfies *Central Hudson*." App., *infra*, 6a (quoting *United States* v. *Edge Broad. Co.*, 509 U.S. 418, 428 (1993)). The court of appeals nevertheless refused to credit the government's interest in preventing the widespread

distribution and sale of drugs that have not been proven safe and effective, on the one hand, and permitting the compounding of drugs in limited circumstances to address the particularized medical needs of individual patients, on the other. The court instead insisted on "convincing evidence" of "the health risks associated with large numbers of patients taking such [compounded] drugs." App., *infra*, 6a-7a. The evidentiary demand imposed by the court of appeals is misplaced, especially in this case. Even as a general matter, this Court has made clear that the government may "justify [advertising and solicitation] restrictions based solely on history, consensus, and 'simple common sense.'" *Lorillard Tobacco Co.* v. *Reilly*, 121 S. Ct. 2404, 2422 (2001) (quoting *Florida Bar* v. *Went For It, Inc.*, 515 U.S. 618, 628 (1995) (citations and internal quotation marks omitted)). As explained more fully below, the government's position here is supported by all of these factors, including considerable regulatory experience and congressional analysis.

Furthermore, the court of appeals' evidentiary demand is particularly inappropriate in this case, because it is based on a rejection of the fundamental premises of the FDCA—that the widespread distribution of drugs that have not first been shown to be safe and effective poses substantial health risks, and that the FDCA's new drug approval requirements are a legitimate and effective means to address those risks. This Court itself has acknowledged the validity of those premises, see *Rutherford*, 442 U.S. at 556-557; *Hynson, Westcott & Dunning*, 412 U.S. at 619, 622, and the court of appeals had no basis to question them here. See also *Warner-Lambert Co.* v. *Heckler*, 787 F.2d 147, 156 (3d Cir. 1986). The Ninth Circuit's apparent insistence that the government introduce evidence in court to establish

the importance of the central purposes of the FDCA was wholly unwarranted.

The court's evidentiary demand appears to have stemmed from its misunderstanding of one of the basic governmental interests underlying Section 353a. That interest is not simply, as the court characterized it, in "preventing widespread compounding." App., *infra*, 7a. Rather, the government's interest is in preventing compounding that is tantamount to manufacturing, which would threaten the integrity of the statutory scheme for ensuring that drugs are found to be safe and effective before they are introduced into commerce. Congress reasonably concluded that, at some point, high-volume compounding of one particular drug product is not meaningfully different from manufacturing that product. See Conf. Rep. 94; S. Rep. 67. At that point, compounders, like ordinary manufacturers, must be required to comply with the FDCA's new drug approval requirements, or those requirements will be substantially undermined. See *Hearings* 35, 59. As the court of appeals itself acknowledged, the government has a substantial interest in preserving the integrity of the drug approval process. App., *infra*, 5a-6a.

Congress also recognized, however, that compounding can meet the particularized medical needs of individual patients who cannot use the versions of drugs that have been approved by the FDA and are commercially available. The court of appeals acknowledged that the government has a substantial interest in permitting limited compounding to meet that need. App., *infra*, 7a-8a. Congress was simply seeking to balance the interest in preserving the integrity of the new drug approval process with the interest in making compounded drug products available in limited circumstances for those patients. See Conf. Rep. 94; S. Rep.

67; 143 Cong. Rec. at S9839 (statements of Sens. Hutchinson and Kennedy). Preserving and advancing those two compelling but competing interests is itself a substantial government interest. See *Edge Broad. Co.*, 509 U.S. at 428 (balancing competing governmental concerns can be a substantial governmental interest for purposes of the *Central Hudson* test).

b. The court of appeals' misapprehension of the government's interests doomed from the outset its application of the third step in the *Central Hudson* analysis. The court of appeals concluded at that step that the government had failed to show that limiting the compounding exemption to pharmacies that do not promote particular compounded products directly and materially advances the government's interests. App., *infra*, 7a-10a. The court understood the government to be arguing that Section "353a's speech restrictions will keep the demand for particular compounded drugs artificially low, and thereby protect unwary consumers." *Id.* at 8a. That was not the goal of Congress in enacting FDAMA. As explained above, Congress concluded that the advertising of a particular compounded drug product to the public reasonably identifies the point at which the interest in preserving the integrity of the drug approval requirement outweighs the interest in protecting the availability of traditional pharmaceutical compounding in response to *individual* medical needs. That congressional determination reflects the fact that advertising and promotion of particular drug products are distinguishing characteristics of drug manufacturing but not traditional, individualized compounding by pharmacies. It is based upon the FDA's prior enforcement experience. And it conforms to the premise of the FDCA that those who promote new drugs in order to realize profits from their

distribution should bear the cost of proving that those drugs are safe and effective for their intended uses before they are marketed. Congress reasonably determined that, when demand is great enough to justify a pharmacy's decision to manufacture large quantities of a particular compounded product and to promote that product through advertising, the pharmacy, like other manufacturers, should be required to bear the costs of complying with the FDCA's approval requirements and demonstrating that the new drug is safe and effective for its intended uses.

The court of appeals also relied on its own assessment that other "safeguards exist to protect the public." App., *infra*, 8a. The provisions of FDAMA on which the court relied, however, confirm the court's misunderstanding of the governmental interests underlying Section 353a. For example, the court noted that, under FDAMA, "[n]o compounded drug may be dispensed without a valid prescription from a licensed physician." *Id.* at 8a-9a (citing 21 U.S.C. 355a(a) (Supp. V 1999)). That requirement alone, however, is insufficient to advance the government's interest in preserving the integrity and safeguarding function of the FDCA's drug approval process, which is based on Congress's judgment that the ultimate determination whether a new drug is safe and effective cannot be left to individual doctors (who cannot by themselves compile and master the necessary information) but instead must be made by the FDA. See *Hynson, Westcott & Dunning*, 412 U.S. at 619, 630; *Warner-Lambert Co.*, 787 F.2d at 156 ("Congress rejected the notion * * * that individual physicians should be left to decide whether particular drugs were effective.").

The court of appeals also observed that a "pharmacist cannot regularly compound drugs that are essentially

copies of a commercially available drug product." App., *infra*, 9a (citing 21 U.S.C. 353a(b)(1)(D) (Supp. V 1999)). Although that limitation furthers the government's interest in preventing pharmacies from manufacturing products that are already available without complying with the FDCA's provisions governing good manufacturing practices, it does not address the problem of the manufacture through widespread compounding of products that are *different* from those that are commercially available. It is the latter form of compounding to which Sections 353a(a) and (c) are addressed, by ensuring that entities that promote the distribution in interstate commerce of *new* drug products will comply with the new drug approval requirements.[2]

The Ninth Circuit also concluded that Section 353a fails the third *Central Hudson* inquiry because, in the court's view, it "is so riddled with exceptions that it is unlikely that the speech restrictions would actually succeed in depressing the volume of compounded drugs." App., *infra*, 9a. The court noted, for example, that Section 353a permits pharmacies to advertise their general compounding services (see 21 U.S.C. 353a(c) (Supp. V 1999)) and does not prevent pharmacies from dispensing significant quantities of drugs intrastate (see 21 U.S.C. 353a(b)(3) (Supp. V 1999)). Contrary to the court of appeals' view, however, those provisions do not

---

[2] Nor do 21 U.S.C. 353a(b)(1)(A) and (B), which limit the substances that pharmacists may use in compounding, address the governmental interest in preventing manufacturing of new drugs under the guise of compounding. Those provisions require that the *ingredients* used in compounded products meet certain quality standards. They do not ensure the safety and effectiveness of the compounded drugs themselves, which are still unapproved new drugs, and they do not operate to prevent compounding activity that is on the scale and in the manner of manufacturing.

impede the accomplishment of Section 353a's purpose of preventing manufacturing under the guise of compounding.

If compounders could actively promote particular compounded drug products without complying with the drug approval requirements, they would enjoy an unfair advantage over traditional drug manufacturers, which would significantly reduce the incentives for manufacturers to expend the resources necessary to prove that their new drugs are safe and effective. Indeed, under such a regime, traditional drug manufacturers could establish their own compounding entities and circumvent the approval process. Advertising that a pharmacy provides general compounding services, however, does not suggest the existence, or foster the growth, of a market for any *particular* compounded drug, and therefore does not significantly distort the incentives of drug manufacturers to comply with the new drug approval requirements. Permitting pharmacies to advertise that they provide compounding services generally thus is consistent with Congress's purpose of ensuring that particular drugs are widely distributed in commerce only after they have been proven to be safe and effective for their intended uses. At the same time, allowing a pharmacy to advertise its general compounding services furthers Congress's interest in preserving the availability of medically necessary treatments for individual patients when demand is insufficient to justify the costs of obtaining advance FDA approval. Section 353a thus does not at all permit "speech that poses the same risks the Government purports to fear." *Greater New Orleans Broad.*, 527 U.S. at 195.

Section 353a(b)(3) likewise does not frustrate the accomplishment of the purposes served by the limitations

on solicitations and advertising. Section 353a(b)(3) provides that a pharmacy may avail itself of the compounding exemption only if it is located in a State that has entered into an agreement with the Secretary that addresses the interstate distribution of inordinate amounts of compounded drugs, or if the pharmacy's total interstate distribution of compounded drug products does not exceed five percent of the total of its prescription orders. See 21 U.S.C. 353a(b)(3) (Supp. V 1999). That provision imposes a restraint in addition to and different in purpose from the advertising and solicitation conditions on the availability of the exemption. The advertising and solicitation limitations prevent the manufacture and marketing of *particular* drug products under the guise of compounding. Section 353a(b)(3) limits the volume of the pharmacy's *overall* interstate sales of compounded drugs in order to ensure that the pharmacy retains its character as a pharmacy rather than a drug manufacturer engaged in interstate commerce. The volume limitation in Section 353a(b)(3) applies only to interstate distributions, so that the States may continue to play their traditional role in regulating pharmacy practice. See 143 Cong. Rec. S12242 (daily ed. Nov. 5, 1997) (Sen. Jeffords) (Congress intended "to establish a rational framework for pharmacy compounding [that] respects the State regulation of pharmacy while allowing an appropriate role for the FDA."). The absence of volume limitations on overall intrastate distributions does not, however, detract from the importance of the advertising and solicitation limitations, which prevent the manufacture of particular drugs under the guise of compounding.

c. Finally, the Ninth Circuit's failure to appreciate the nature of the government's interests also led to its erroneous conclusion that Sections 353a(a) and (c) are

not sufficiently tailored to satisfy the fourth step of the *Central Hudson* inquiry. As this Court has recently reiterated, "'the least restrictive means' is not the standard; instead, the case law requires a reasonable 'fit between the legislature's ends and the means chosen to accomplish those ends.'" *Lorillard Tobacco Co.*, 121 S. Ct. at 2422 (quoting *Went For It, Inc.*, 515 U.S. at 632 (quoting in turn *Board of Trustees* v. *Fox*, 492 U.S. 469, 480 (1989))).

The court of appeals incorrectly concluded that "clear alternatives exist that can advance the government's asserted interest in a manner far less intrusive to the pharmacists' free speech rights." App., *infra*, 10a. On the contrary, the alternatives suggested by the court—requiring "disclaimers on compounded drugs explaining that they had not been subject to FDA approval," or subjecting all compounded drug products to the FDCA's new drug approval requirements, *ibid.*—would not only fail to advance, but would substantially hinder, the accomplishment of the purposes of Sections 353a(a) and (c).

Reliance on disclaimers is fundamentally inconsistent with the purposes of the FDCA's approval requirements. Congress has determined that public health and safety are best protected by requiring manufacturers to demonstrate to the FDA that their drugs are safe and effective for their intended uses *before* they are distributed widely in commerce. See *Hynson, Westcott & Dunning*, 412 U.S. at 619, 630. Disclaimers would not accomplish that purpose.

The other alternative suggested by the court of appeals—subjecting all compounded drugs to the new drug approval process—would be directly contrary to Congress's purpose of making compounded drugs available in the limited and individualized circumstances in which a specific patient cannot use the commercially available version of the drug. The court of appeals thus erred in concluding that Section 353a is not narrowly tailored to achieve the government's substantial interest in balancing the availability of compounding in response to the particular medical needs of individual patients with preventing manufacturing under the guise of compounding, which would threaten the integrity of the drug approval requirements.

3. The court of appeals has held an Act of Congress unconstitutional. That action alone warrants this Court's review. See *Gainey*, 380 U.S. at 65. The solicitation and advertising limitations in Sections 353a(a) and (c) were enacted by Congress as essential conditions on the availability of the exemption from the FDCA's new drug approval and other requirements. The court of appeals invalidated those limitations based on its misconception of the statutory provisions involved and its mistaken view of the First Amendment's application in the critical context of protecting the public health and safety. As we have explained above, the court of appeals' decision upsets the careful balance that Congress struck in Section 353a in specifying the point at which drug products should be subject to the FDCA's generally applicable new drug approval requirements. Those requirements are the linchpin of the Nation's laws regulating the manufacturing and distribution of drugs, and thus a central component of Congress's efforts in the FDCA to protect the public health and safety.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

THEODORE B. OLSON
Solicitor General

STUART E. SCHIFFER
Acting Assistant Attorney General

EDWIN S. KNEEDLER
Deputy Solicitor General

MATTHEW D. ROBERTS
Assistant to the Solicitor General

DOUGLAS N. LETTER
Attorney

AUGUST 2001

APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

No. 99-17424

WESTERN STATES MEDICAL CENTER, A NEVADA CORPORATION; WOMEN'S INTERNATIONAL PHARMACY, A WISCONSIN CORPORATION; HEALTH PHARMACY, A WISCONSIN CORPORATION; APOTHECURE, A TEXAS CORPORATION; COLLEGE PHARMACY, A COLORADO CORPORATION; LAKESIDE PHARMACY, A TENNESSEE CORPORATION; WEDGEWOOD VILLAGE PHARMACY, A NEW JERSEY CORPORATION, PLAINTIFFS-APPELLEES

v.

DONNA E. SHALALA, IN HER OFFICIAL CAPACITY AS SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; JANE E. HENNEY, M.D., IN HER OFFICIAL CAPACITY AS COMMISSIONER, DEFENDANTS-APPELLANTS

Appeal from the United States District Court
for the District of Nevada
David A. Ezra, District Judge, Presiding
D.C. No. CV-98-01650-DAE(RLH)

Argued and Submitted: Dec. 12, 2000
Filed: Feb. 6, 2001

Before: SCHROEDER, Chief Judge, HALL, and W. FLETCHER, Circuit Judges.

CYNTHIA HOLCOMB HALL, Circuit Judge.

This appeal requires us to assess the constitutionality of two subsections of the Food and Drug Administration Modernization Act of 1997 ("FDAMA"), 21 U.S.C. § 353a. Subsections §§ 353a(a) and (c) of FDAMA prohibit drug providers from promoting or advertising particular compounded drugs. In return, the providers are exempted from the standard drug approval requirements imposed by the Food and Drug Administration. Plaintiffs seek to enjoin the enforcement of these subsections, contending that they violate the First Amendment's guarantee of free speech. The district court agreed with Plaintiffs and granted their motion for summary judgment in a published opinion. *See Western States Medical Ctr.* v. *Shalala*, 69 F. Supp. 2d 1288 (D. Nev. 1999). The district court exercised jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1361. We have jurisdiction over this appeal pursuant to 28 U.S.C. § 1291.

I

Plaintiffs are a group of licensed pharmacies. They have prepared written promotional materials that they distribute by mail and at medical conferences to inform patients and physicians of the uses and effectiveness of specific compounded drugs. "Compounding" is a process in which a pharmacist mixes ingredients to create a medication for an individual patient. Compounding is typically used to prepare medications that are not commercially available, such as a medication for a patient

who is allergic to an ingredient in a mass-produced product. Pharmacists can provide compounded drugs to individual patients only upon receipt of a valid prescription. *See* 21 U.S.C. § 353a(a).

The Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301-397, regulates drug manufacturing, marketing, and distribution. It invests the Food and Drug Administration ("FDA") with enforcement powers to make sure that the regulations are followed. In 1997, Congress amended the FDCA to exempt compounding from certain requirements of the FDCA, but only if the compounding pharmacies followed several conditions, including refraining from promoting particular compounded drugs. The new legislation sets out several restrictions on compounding including prohibitions on advertisements, like those of the Plaintiffs, that promote particular compounded drugs. *See* 21 U.S.C. §§ 353a(a) and (c).[3] Pharmacists

---

[3] The statutes provide:

> [Some FDCA requirements do not] apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient . . . .

21 U.S.C. § 353a(a).

> A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.

21 U.S.C. § 353a(c).

may, however, inform the public that they offer general compounding services. *See* 21 U.S.C. § 353a(c).

Plaintiffs challenged FDAMA's advertising and solicitation restrictions in district court. They contended that the restrictions violate the Free Speech Clause of the First Amendment. In a well-reasoned opinion, the district court granted Plaintiff's motion for summary judgment, holding that the restrictions do not meet the test for acceptable government regulation of commercial speech set forth in *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557, 566, 100 S. Ct. 2343, 65 L. Ed. 2d 341 (1980). The district court also held that the unconstitutional provisions were severable from the rest of FDAMA. This Court reviews the district court's grant of summary judgment de novo. *See Gutowsky* v. *County of Placer*, 108 F.3d 256, 259 (9th Cir. 1997). "The evidence must be viewed in the light most favorable to the nonmoving party to determine whether there are any genuine issues of material fact for trial, and whether the district court correctly applied the relevant substantive law." *Federal Deposit Ins. Corp.* v. *O'Melveny & Meyers*, 969 F.2d 744, 747 (9th Cir. 1992).

II

In *Central Hudson*, the Supreme Court set out a four-part test for determining the constitutionality of a government restriction on commercial speech. The court must determine whether: 1) the regulated speech is misleading or concerns unlawful activity; 2) the government has asserted a "substantial" interest in restricting the speech; 3) the government has demonstrated that the regulation "directly advances" the asserted interest; and 4) the restriction is not more

extensive than necessary to achieve the asserted governmental interest. *See Central Hudson*, 447 U.S. at 566, 100 S. Ct. 2343. Although the government has asserted substantial interests, they have failed to demonstrate that the speech restrictions directly advance those interests or that they are narrowly tailored to those interests.

A

The First Amendment does not protect commercial speech that is "inherently misleading" or concerns unlawful activity. *See id.* at 563-64, 100 S. Ct. 2343. On appeal, the government does not contend that the prohibited speech is unlawful or misleading, and there is no indication in the record that Plaintiffs' advertisements are untruthful. Therefore, the restricted speech must be evaluated according to the other three *Central Hudson* factors.

B

Under the second part of the *Central Hudson* test, the speech restriction must serve a "substantial" government interest. In the district court, the government argued that the challenged restrictions served three substantial interests: 1) protecting the public health and safety; 2) preserving the integrity of the drug approval process; and 3) balancing the need to preserve drug compounding for individual patients with particularized needs while preventing widespread distribution of compounded drugs. The district court determined that the first two interests were substantial and satisfied the second prong of the *Central Hudson* test. Because "the Government has a significant interest in protecting the health, safety, and welfare of its

citizens," we agree that the first two interests are substantial. *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 485, 115 S. Ct. 1585, 131 L. Ed. 2d 532 (1995).

The third asserted interest was "insufficiently clear" to the district court. *Western States*, 69 F. Supp. 2d at 1303. The court reasoned that for an interest in balancing competing goals to be substantial, the goals themselves must be substantial. *See id.* at 1302. The court agreed that the goal of ensuring the continued availability of compounded drugs to individual patients was a substantial concern, but was not convinced that the government had a substantial interest in preventing widespread compounding. It held that if the government could not offer an adequate rationale for its goal of preventing widespread distribution of compounded drugs, then the government did not have a substantial interest in balancing this concern with the need for continued access to such drugs. *See id.* at 1302-03.

The government's effort to balance competing goals can be a substantial interest worthy of government protection. *See United States* v. *Edge Broadcasting Co.*, 509 U.S. 418, 428, 113 S. Ct. 2696, 125 L. Ed. 2d 345 (1993) (holding that the "congressional policy of balancing the interests of lottery and non-lottery States is the substantial government interest that satisfies *Central Hudson*"). But the government must supply a compelling argument or convincing evidence that it has a substantial interest in achieving both goals. The government cannot carry its burden by "mere speculation or conjecture." *Edenfield* v. *Fane*, 507 U.S. 761, 770-71, 113 S. Ct. 1792, 123 L. Ed. 2d 543 (1993); *cf. Florida Bar* v. *Went For It, Inc.*, 515 U.S. 618, 624, 115 S. Ct. 2371, 132 L. Ed. 2d 541 (1995) (crediting the state's interest

as substantial on the basis of a two-year study containing statistical and anecdotal evidence).

We agree with the district court that the government has not met its burden. There is insufficient evidence in the record to conclude that the government has a substantial interest in preventing widespread compounding. The government asserts that increased distribution of compounded drugs is dangerous because of the health risks associated with large numbers of patients taking such drugs. The government neither explains nor supports this contention. In fact, most of the evidence runs to the contrary. Compounding is not only legal under state law, but most states require their pharmacists to know how to compound. *See* Sen. Rep. No. 105-43, at 64 (1997). The government has failed to show that its interest in striking a balance between ensuring compounding availability and limiting widespread compounding is substantial. The only substantial interests asserted by the government are protecting the public's health and preserving the integrity of the drug approval process.

C

Under the third *Central Hudson* factor, the speech regulation must "directly advance" the government interest. In essence, the government argues that the speech restrictions are necessary to prevent an increase in the demand for compounded drugs that would be injurious to the public health. But the government's argument falls short of what is required to show that the speech restrictions will protect the public. The government has not offered evidence or arguments to explain sufficiently why such restrictions will reduce the type of consumption of compounded drugs that is

harmful, and even admits that it has a substantial interest in ensuring the availability of compounded drugs.

The government bears the burden of showing that its regulation will advance its interest "to a material degree." *See 44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484, 505, 116 S. Ct. 1495, 134 L. Ed. 2d 711 (1996). In *44 Liquormart*, the Supreme Court held that a state statute prohibiting advertisement of liquor prices violated the First Amendment. The Court agreed with the State that "common sense supports the conclusion that a prohibition against price advertising . . . will tend to mitigate competition and maintain prices at a higher level than would prevail in a completely free market." *Id.* at 505, 116 S. Ct. 1495. But the Court disagreed with the State's argument that the prohibition would advance the State's interest in promoting temperance and reducing demand "to a material degree." The Court explained that it required evidentiary support for such an argument, not mere speculation. *See id.* "Such speculation certainly does not suffice when the State takes aim at accurate commercial information for paternalistic ends." *Id.* at 507, 116 S. Ct. 1495. Similarly, the government in this case contends that § 353a's speech restrictions will keep the demand for particular compounded drugs artificially low, and thereby protect unwary consumers. The government offers no evidence demonstrating that its restrictions would succeed in striking the balance it claims is a substantial interest, or even would protect the public health.

Without the advertising restrictions, other safeguards exist to protect the public. No compounded drug may be dispensed without a valid prescription from a licensed physician to an individual patient. *See*

§ 353a(a). FDAMA sets out specific requirements for the substances that can be used by the pharmacist to fashion a compounded drug. *See* § 353a(b)(1). A pharmacist cannot regularly compound drugs that are essentially copies of a commercially available drug product. *See* § 353a(b)(1)(D).

In addition, FDAMA is so riddled with exceptions that it is unlikely that the speech restrictions would actually succeed in depressing the volume of compounded drugs. The exceptions also demonstrate that the restrictions do not directly advance the government's interest in maintaining the integrity of the drug approval process. Under the statute, pharmacists can advertise their compounding services and promote their skills at medical trade events so long as they do not promote the compounding of any *particular* drug. It seems obvious that advertising that informs physicians that a pharmacy is available to compound drugs is likely to increase demand for compounding. Moreover, even with the ban on specific advertising, FDAMA provides significant incentives for pharmacies to increase their drug compounding business. The statute allows compounded drugs to constitute up to five percent of a pharmacy's interstate drug distributions and 100 percent of its intrastate drug distributions. If a pharmacy has a Memorandum of Understanding with the Secretary of Health and Human Services, up to twenty percent of its interstate drug distributions can be in the form of compounded drugs. *See* § 353a(b)(3). Under FDAMA, a pharmacist can call a physician and recommend a drug compound when a patient comes in with a prescription for a commercial drug and provides information to the pharmacist that indicates that the patient might require a compounded product. When

exemptions and inconsistencies counteract the alleged purpose of a speech restriction, the restriction fails the direct advancement test. *See Greater New Orleans Broadcasting Ass'n* v. *U.S.*, 527 U.S. 173, 190, 119 S. Ct. 1923, 144 L. Ed. 2d 161 (1999); *Rubin*, 514 U.S. at 488-89, 115 S. Ct. 1585 (1995).

D

Finally, the speech restrictions fail the fourth *Central Hudson* factor; they are more extensive than necessary to achieve the asserted government interest. If clear alternatives exist that can advance the government's asserted interest in a manner far less intrusive to the pharmacists' free speech rights, then the restrictions are invalid. *See Coors Brewing*, 514 U.S. at 490-91, 115 S. Ct. 1585; *Project 80's, Inc.* v. *City of Pocatello*, 942 F.2d 635, 637 (9th Cir. 1991). The district court proposed either disclaimers on compounded drugs explaining that they had not been subject to FDA approval or a full-blown safety review like that imposed on manufactured drugs as alternatives that would be far less intrusive to free speech. *See Western States*, 69 F. Supp. 2d at 1308-09. Disclaimers would satisfy the government's substantial interest in preventing consumers from being misled into taking unsafe drugs. Full-scale FDA review of compounded drugs would satisfy the government's interest in protecting the public health and serve as a much more precise way of preserving the integrity of the drug approval process. *See Project 80's*, 942 F.2d at 638 (stating that where there are "far less restrictive and more precise means" to achieve the desired end, the speech restriction is more extensive than necessary and fails the fourth *Central Hudson* factor.)

The government contends that the district court's suggested alternatives are useless since they do not address the government's substantial interest in balancing the availability of compounded drugs with the need to limit their widespread "manufacture." But the district court's alternatives are viable because the government's interest in balancing two competing goals failed to meet the second prong of *Central Hudson*. The alternatives do offer credible solutions for the government's substantial interests in safeguarding the public health and maintaining the integrity of the drug approval process.

Even if the district court had not proposed compelling alternatives and the government had marshaled sufficient evidence to show that compounded drugs are dangerous and their volume should be limited, prohibitions on truthful speech are still strongly disfavored. "We have never held that commercial speech may be suppressed in order to further the State's interest in discouraging purchases of the underlying product that is advertised." *Central Hudson*, 447 U.S. at 574, 100 S. Ct. 2343 (Blackmun, J., concurring). In *44 Liquormart*, the Court explained:

> Precisely because bans against truthful, nonmisleading commercial speech rarely seek to protect consumers from deception or overreaching, they usually rest solely on the offensive assumption that the public will respond "irrationally" to the truth. The First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good.

517 U.S. at 503, 116 S. Ct. 1495. Government prohibitions of truthful commercial messages are "particularly dangerous" and deserve "rigorous review." *Id.* at 501, 116 S. Ct. 1495. The government has failed to support adequately its assertion that lower demand for compounded drugs will protect the public. Workable alternatives to the speech restrictions exist. Therefore, FDAMA's speech restrictions are more extensive than necessary.

III

Sections 353a(a) and (c) cannot be severed from the rest of FDAMA unless Congress would have enacted the constitutional provisions of FDAMA absent the unconstitutional provisions. *See Alaska Airlines* v. *Brock*, 480 U.S. 678, 685, 107 S. Ct. 1476, 94 L. Ed. 2d 661 (1987); *Board of Natural Resources* v. *Brown*, 992 F.2d 937, 948 (9th Cir. 1993). A statute's unconstitutional provisions are not severable if the entire statute is designed to strike a balance between competing interests. *See United States* v. *Spokane Tribe of Indians*, 139 F.3d 1297, 1301 (9th Cir. 1998). FDAMA's legislative history demonstrates that Congress intended to provide access to compounded drugs while preventing pharmacies from making an end run around the FDA's drug manufacturing requirements.

The first legislative proposal to address pharmacy compounding appeared in the House of Representatives in 1996. That bill would have exempted pharmacy compounding from FDCA requirements without restrictions on advertising specific compounded products. *See* H.R. 3199, 104th Cong. § 18 (Apr. 30, 1996). FDA Commissioner David Kessler expressed concern with the bill's lack of safeguards, and the possibility of a massive

increase in the number of drugs available that did not meet FDA standards:

> The [bill] has no constraints on the volume of compounding. It is likely to encourage large-scale manufacturing under the guise of pharmacy compounding. It would allow bulk drug suppliers or drug manufacturers to circumvent the approval requirements of the Act by shipping bulk drug substances to pharmacies for reconstituting or other processing. A shadow industry of unapproved generic drugs is likely to develop. Moreover, the exemptions would allow potentially dangerous compounding.

FDA Reform Legislation: Hearings Before the Subcomm. on Health and Environ. of the House Comm. on Commerce, 104th Cong. 31, 125 (May 1 and 2, 1996) (statement of Hon. David A. Kessler).

Subsequent versions of the legislation responded to the FDA Commissioner's concerns. The new House bill provided that the compounded products would be exempt from FDCA requirements only if the compounding pharmacist "does no more than advertise or otherwise promote the compounding service and does not advertise or otherwise promote the compounding of a particular drug or device." H.R. 1411, 105th Cong. § 17 (Apr. 23, 1997). A similar Senate bill tied exemption from FDCA requirements to a prohibition on advertising particular compounded drugs. *See* S. 830, 105th Cong., § 809 (July 1, 1997).

Evidence in the legislative record interpreting the final legislation demonstrates that Congress meant to exempt compounding pharmacists from FDCA requirements only in return for a prohibition on the promotion

of specific compounded drugs. A House report explained that FDAMA was designed to "ensure continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." H.R. Conf. Rep. No. 105-399. Senator Kennedy noted that "some of [FDAMA's] conditions are intended to ensure that the volume of compounding does not approach that ordinarily associated with drug manufacturing." 143 Cong. Rec. S9840 (Daily ed. Sept. 24, 1997). The President's comments upon signing FDAMA into law reflect a concern with striking a balance between compounding and manufacturing: "The Act will also resolve the issue of pharmacy compounding-the process of making customized medicines-so that legitimate pharmacy compounding is allowed, while the manufacture of unapproved drugs is not." Statement on Signing the Food and Drug Administration Modernization Act of 1997, 33 Weekly Comp. Pres. Doc. 1885 (Nov. 21, 1997). Given these statements and the decision by both houses of Congress to add specific provisions to address the advertising or promotion of compounded products, we believe that Congress would not have passed FDAMA absent the restrictions on commercial speech.

The existence of a severability clause at § 1391 of the FDCA does not change our interpretation of the legislative history.[4] It is true that the presence of a

[4] The clause reads:

> If any provision of this Act is declared unconstitutional, or the applicability thereof to any person or circumstance is held invalid, the constitutionality of the remainder of the Act and the applicability thereof to other persons and circumstances shall not be affected thereby.

severability clause creates a presumption that Congress did not intend for the validity of a statute to depend on the survival of its constitutionally offensive provisions. *See Alaska Airlines* v. *Brock*, 480 U.S. 678, 686, 107 S. Ct. 1476, 94 L. Ed. 2d 661 (1987). But that presumption is not conclusive. *See id.* Because Congress approved this severability clause *before* FDAMA's passage, it is less compelling evidence of legislative intent than a clause enacted simultaneously with FDAMA. Congress may have intended the original provisions of the FDCA to be severable, but meant for FDAMA's provisions to stand or fall together. Given the evidence in the legislative history of Congress's desire to facilitate drug compounding while not allowing for widespread creation of drugs that have not been FDA approved, the FDCA's severability clause is not persuasive.

IV

Thus, we hold that § 353a(a) and § 353a(c)'s restrictions on commercial speech violate the First Amendment. These provisions may not be severed from the rest of the provisions in § 353a. Accordingly, § 353a is invalid in its entirety.

AFFIRMED IN PART, REVERSED IN PART.

21 U.S.C. § 391.

APPENDIX B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEVADA

No. CV-S-98-01650(DAE)(RLH)

WESTERN STATES MEDICAL CENTER, A NEVADA CORPORATION; WOMEN'S INTERNATIONAL PHARMACY, A WISCONSIN CORPORATION; HEALTH PHARMACY, A WISCONSIN CORPORATION; APOTHECURE, A TEXAS CORPORATION; COLLEGE PHARMACY, A COLORADO CORPORATION; LAKESIDE PHARMACY, A TENNESSEE CORPORATION; WEDGEWOOD VILLAGE PHARMACY, A NEW JERSEY CORPORATION, PLAINTIFFS

v.

DONNA E. SHALALA, IN HER OFFICIAL CAPACITY AS SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; JANE E. HENNEY, M.D., IN HER OFFICIAL CAPACITY AS COMMISSIONER, DEFENDANTS

Filed: Sept. 16, 1999

ORDER DENYING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT AND GRANTING PLAINTIFFS' CROSS-MOTION FOR SUMMARY JUDGMENT

DAVID ALAN EZRA, Chief Judge.

The court heard the parties' motions on June 22, 1999. Michael A. Reiter, Esq., and Howard M. Hoffman, Esq., appeared at the hearing on behalf of

Plaintiffs; Gerald C. Kell, Esq., Patricia J. Kaeding, Esq., and Blaine T. Welsh, Esq., appeared at the hearing on behalf of Defendants. After reviewing the Motions and the supporting and opposing memoranda, the court DENIES Defendants' Motion for Summary Judgment and GRANTS Plaintiffs' Cross-Motion for Summary Judgment.

I. *BACKGROUND*

This case involves a First Amendment challenge to Section 503A of the Food and Drug Modernization Act of 1997 (the "Modernization Act"), codified at 21 U.S.C. § 353a ("§ 353a"). The Modernization Act exempts "compounded drugs" from the standard drug approval requirements imposed by the Food and Drug Administration ("FDA"). However, §§ 353a(a) and (c) condition this exemption on drug providers agreeing to not promote or advertise particular compounded drugs. Plaintiffs are licensed pharmacists seeking to enjoin the enforcement of these subsections of § 353a, contending that they violate the First Amendment's guarantee of free speech.[5]

---

[5] Plaintiffs' challenge here is focused on §§ 353a(a) and (c), which, taken together, restrict the advertisement or promotion of compounded drugs as well as the solicitation of business associated with their production. However, in their Complaint, Plaintiffs also challenge § 353a(b)(3), which limits the distribution of compounded drugs to no more than five percent of the total prescription orders dispensed outside the state, unless a Memorandum of Understanding ("MOU") is developed between a state and the Secretary of Health and Human Services which "addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounding drug products distributed outside such States . . . ." In such a case, up to 20% of pharmacists' total

A. *Factual Background*

Compounding is the process by which a pharmacist combines, mixes or alters ingredients to create a medication that serves the unique needs of specific patients. Pharmacists may provide compounded drugs to individual patients upon receipt of a valid prescription. Such drugs are produced for a variety of reasons, such as when the patient is allergic to an ingredient in the product or when the product is not available in the proper dosage. It is a process that is taught as part of the standard curriculum at most pharmacy schools, and most states have laws requiring that pharmacists have sufficient education and equipment to provide some compounding services.

Plaintiffs are eight licensed pharmacies located in seven states. In addition to providing traditional pharmaceutical services, they regularly compound drugs in order to meet the specific needs of individual patients. To accomplish this task, Plaintiffs maintain that they have each pursued individual specializations in the compounding of certain drugs. As a result, compounded drugs represent between 60% and 90% of Plaintiffs' total drug orders.

---

orders distributed in interstate commerce may constitute compounded drugs. To this date, the Secretary has not developed an MOU with any state. Moreover, the Secretary issued a "Guidance for Industry on Enforcement Policy during Implementation for Section 503A for the Federal Food, Drug and Cosmetic Act," which states that the FDA will exercise its discretion to not enforce § [353a(b)(3)] "[until] at least 90 days after the standard MOU is finalized and made available to the States for their consideration and signature." Because the FDA has agreed not to enforce this Section, Plaintiffs are not currently seeking injunctive relief with respect to § 353a(b)(3).

According to Plaintiffs, they have traditionally advertised their compounding services in order to both promote their products and inform physicians and patients of the variety of available compounded drugs. Plaintiffs explain that the compounding process requires them to consult with physicians and patients, and in some cases, make recommendations about the proper combination of drugs. Accordingly, they have prepared written promotional materials that they distribute both by mail and at medical conferences, and they often include studies and other research to inform consumers and physicians of the uses and effectiveness of specific compounded drugs.

B. *Statutory History and Framework*

The Federal Food, Drug and Cosmetic Act (the "FDC Act"), 21 U.S.C. § 355(a), imposes stringent conditions on the manufacture and distribution of new drugs.[6] The FDC Act imposes numerous requirements on the approval of new drugs, and provides that "[n]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug." § 355(a). All new drugs must comply with these requirements unless Congress has provided an explicit exemption.

Historically, while the FDA has subjected new drugs to its requirements, it has permitted pharmacists to

---

[6] "New drug" is defined as "any drug . . . generally recognized . . . as safe and effective for use under the conditions prescribed. . . ." 21 U.S.C. § 321(p). To obtain FDA approval of a new drug, the manufacturer must demonstrate to the FDA that the drug is safe and effective for each of its purported uses. 21 U.S.C. § 355(b).

compound drugs without meeting these stringent safety standards. In accordance with this policy, prior to the enactment of the Modernization Act in 1997, the FDA had never exercised its authority to subject compounded drugs to the FDC Act's requirements. However, the FDA had expressed concern over efforts by pharmacists and other drug providers to manufacture drugs under the guise of compounding. In 1992, the FDA issued a Compliance Policy Guide ("CPG") that reflected the FDA's policy regarding efforts to manufacture drugs without obtaining FDA approval. The CPG set forth nine factors the FDA used to determine whether a drug provider's efforts to produce a particular drug justified the FDA's exercise of enforcement action under the FDC Act. These factors included "[s]oliciting business (e.g., promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products," and "[d]istributing inordinate amounts of compounded products out of state." CPG at 153-54, attached as Exhibit A to Defendants' Motion for Summary Judgment. The CPG explained that such actions were more consistent with manufacturing than compounding, and enforcement of FDA regulations was thus necessary to prevent the "very real potential for causing harm to the public health when drug products are manufactured and distributed in commercial amounts without FDA's approval." CPG at 152.

In 1997, Congress formally recognized this policy by enacting the Modernization Act of 1997. Under the Modernization Act, pharmacists are free to produce compounded drugs without meeting the FDA's restrictive regulations, as long as they satisfy several conditions. First, under subsection (a), the drug product

must be compounded "for an identified individual patient based on the unsolicited receipt of a valid prescription order." Subsection (b) imposes numerous standards on the quality of the ingredients of the compounded drug, requiring, *inter alia*, that the drug product be compounded from a list of approved drug substances that have not been deemed unsafe or inappropriate for compounding. Finally, under subsection (c), a drug may be compounded "only if the pharmacy, licensed pharmacist or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug."

On November 19, 1998, Plaintiffs filed their Complaint and Motion for Temporary Restraining Order, seeking injunctive and declaratory relief. They contended that because §§ 353a(a) and (c) allow pharmacists to compound drugs only if they forego the advertising and promotion of their products, these subsections represent an unconstitutional condition in violation of the free speech clause of the First Amendment. On November 20, 1998, Plaintiffs filed a Motion for Temporary Restraining Order and Preliminary Injunction, requesting that the court enjoin the enforcement of the speech-related restrictions in §§ 353a(a) and (c). On December 18, 1998, after an evidentiary hearing held on December 4, 1998, the court granted Plaintiffs' Motion in part and temporarily restrained the Government from enforcing § 353a ("TRO Order"). The parties stipulated to the extension of the TRO Order, pending resolution of the Summary Judgment Motions addressed here.

II. *STANDARD OF REVIEW*

Rule 56(c) of the Federal Rules of Civil Procedure provides that summary judgment shall be entered when:

> . . . the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law.

The moving party has the initial burden of "identifying for the court those portions of the materials on file that it believes demonstrate the absence of any genuine issue of material fact." *T.W. Elec. Serv., Inc.* v. *Pacific Elec. Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir. 1987) (citing *Celotex Corp.* v. *Catrett*, 477 U.S. 317, 323, 106 S. Ct. 2548, 91 L. Ed. 2d 265 (1986)). The movant must be able to show "the absence of a material and triable issue of fact," *Richards* v. *Neilsen Freight Lines*, 810 F.2d 898, 902 (9th Cir. 1987), although it need not necessarily advance affidavits or similar materials to negate the existence of an issue on which the nonmoving party will bear the burden of proof at trial. *Celotex*, 477 U.S. at 323, 106 S. Ct. 2548. *But cf., id.*, at 328, 106 S. Ct. 2548 (White, J., concurring).

If the moving party meets its burden, then the opposing party may not defeat a motion for summary judgment in the absence of any significant probative evidence tending to support his legal theory. *Commodity Futures Trading Comm'n* v. *Savage*, 611 F.2d 270, 282 (9th Cir. 1979). The opposing party cannot stand on his pleadings, nor can he simply assert that he will be able to discredit the movant's evidence at trial.

See T.W. Elec., 809 F.2d at 630. Similarly, legal memoranda and oral argument are not evidence and do not create issues of fact capable of defeating an otherwise valid motion for summary judgment. *British Airways Bd.* v. *Boeing Co.*, 585 F.2d 946, 952 (9th Cir. 1978), *cert. denied*, 440 U.S. 981, 99 S. Ct. 1790, 60 L. Ed. 2d 241 (1979). Moreover, "if the factual context makes the nonmoving party's claim *implausible*, that party must come forward with more persuasive evidence than would otherwise be necessary to show that there is a genuine issue for trial." *California Architectural Bldg. Products, Inc.* v. *Franciscan Ceramics*, 818 F.2d 1466, 1468 (9th Cir. 1987), (citing *Matsushita Elec. Indus. Co., Ltd.* v. *Zenith Radio Corp.*, 475 U.S. 574, 587, 106 S. Ct. 1348, 89 L. Ed. 2d 538 (1986)) (original emphasis).

The standard for a grant of summary judgment reflects the standard governing the grant of a directed verdict. *See Eisenberg* v. *Insurance Co. of North America*, 815 F.2d 1285, 1289 (9th Cir. 1987) (citing *Anderson* v. *Liberty Lobby, Inc.*, 477 U.S. 242, 250, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986)). Thus, the question is whether "reasonable minds could differ as to the import of the evidence." *Eisenberg*, 815 F.2d at 1289.

However, when "direct evidence" produced by the moving party conflicts with "direct evidence" produced by the party opposing summary judgment, "the judge must assume the truth of the evidence set forth by the nonmoving party with respect to that fact." *T.W. Elec.*, 809 F.2d at 631. Also, inferences from the facts must be drawn in the light most favorable to the nonmoving party. *Id.* These inferences may be drawn both from underlying facts that are not in dispute, as well as from

disputed facts which the judge is required to resolve in favor of the nonmoving party. *Id.*

III. *DISCUSSION*

In their Complaint, Plaintiffs argue that the restrictions on advertising and promoting compounded drugs contained in subsections (a) and (c) of the Modernization Act violate Plaintiffs' First Amendment rights to free speech. They challenge these sections on two bases: 1) they are unconstitutional on their face; and 2) they are unconstitutional as applied to Plaintiffs.

Defendants advance two arguments in support of the instant Motion for Summary Judgment. First, they contend that Plaintiffs lack standing to bring their "as-applied" challenge to § 353a, as they have not demonstrated that it either has been or will be applied to them. Second, they argue that § 353a is a valid limitation on Plaintiffs' free speech rights, and therefore, does not violate the First Amendment. The court begins with the preliminary issue of standing, and then turns to the constitutionality of § 353a.

A. *Standing*

A plaintiff may challenge a regulation, ordinance or other government action on the grounds that it is unconstitutional on its face or unconstitutional as it applies to the plaintiff. *Bd. of Trustees of the State Univ. of New York*, 492 U.S. 469, 482, 109 S. Ct. 3028, 106 L. Ed. 2d 388 (1989); *Gaudiya Vaishnava Society* v. *City of Monterey*, 7 F. Supp. 2d 1034, 1041 (N.D. Cal. 1998). An ordinance will be deemed facially unconstitutional in either of two cases: "[E]ither . . . it is unconstitutional in every conceivable application, or . . . it seeks to prohibit such a broad range of

protected conduct that it is unconstitutionally overbroad." *Members of City Council* v. *Vincent*, 466 U.S. 789, 104 S. Ct. 2118, 80 L. Ed. 2d 772 (1984) ("*Vincent*"). Where a regulation implicates only commercial speech, however, parties may generally not lodge a facial challenge to a regulation of commercial speech on overbreadth grounds. *See Village of Hoffman Estates* v. *Flipside, Hoffman Estates, Inc.*, 455 U.S. 489, 497, 102 S. Ct. 1186, 71 L. Ed. 2d 362 (1982); *Washington Mercantile Ass'n* v. *Williams*, 733 F.2d 687, 689 (9th Cir. 1984). Therefore, Plaintiffs' facial challenge must be made on the ground that § 353a is unconstitutional in "every conceivable application."

Plaintiffs may also challenge the constitutionality of a statute as it applies to them. "An as-applied challenge contends that the law is unconstitutional as applied to the litigant's particular speech activity, even though the law may be capable of valid application to others." *Foti* v. *City of Menlo Park*, 146 F.3d 629, 635 (9th Cir. 1998). "A determination that an ordinance's application is unconstitutional as applied to a particular plaintiff does not necessarily render the ordinance invalid, it only invalidates the particular application of the ordinance." *Gaudiya Vaishnava Society* v. *City of Monterey*, [7 F. Supp. 2d at] 1041 (N.D. Cal. 1998).

Whether a party asserts a facial or as-applied challenge, Article III of the United States Constitution requires that there be an actual case or controversy before the court. *See Flast* v. *Cohen*, 392 U.S. 83, 94-101, 88 S. Ct. 1942, 20 L. Ed. 2d 947 (1968). To satisfy the case or controversy requirement, plaintiffs must demonstrate that they have suffered an actual or threatened injury as a result of the challenged conduct and that the injury will be redressed by a favorable

decision. *See Valley Forge Christian College* v. *Americans United for Separation of Church and State, Inc.*, 454 U.S. 464, 472, 102 S. Ct. 752, 70 L. Ed. 2d 700 (1982). A party who fails to meet this requirement lacks standing to bring its claims. *See Secretary of State of Maryland* v. *Munson*, 467 U.S. 947, 955, 104 S. Ct. 2839, 81 L. Ed. 2d 786 (1984).

In this case, Plaintiffs advance a "pre-enforcement" challenge to § 353a, explaining that they intend to engage in conduct that will put them within the statute's reach and § 353a thus poses a threat of injury. Defendants do not contest Plaintiffs' right to bring a *facial* pre-enforcement challenge. Defendants argue, however, that Plaintiffs may not assert an as-applied challenge because the statute has not actually been applied to them. Thus, at bottom, Defendants contend that facial pre-enforcement challenges and as-applied pre-enforcement challenges are subject to different standing requirements.

Courts discussing standing to bring "pre-enforcement" challenges have not typically differentiated between as-applied and facial challenges. Rather, they have concluded generally that standing to bring a pre-enforcement challenge exists when the "plaintiff has alleged an intention to engage in a course of conduct arguably affected with a constitutional interest, but proscribed by a statute, and there exists a credible threat of prosecution." *Babbitt* v. *United Farm Workers Nat'l Union*, 442 U.S. 289, 298, 99 S. Ct. 2301, 60 L. Ed. 2d 895 (1979); *see also Doucette* v. *City of Santa Monica*, 955 F. Supp. 1192 (C.D. Cal. 1997).

The Ninth Circuit has explained that unless a plaintiff lodges an overbreadth attack, which permits the plaintiff to assert the interests of third parties, the

plaintiff must meet traditional standing requirements. *N.A.A.C.P., Western Region* v. *City of Richmond*, 743 F.2d 1346, 1352 (9th Cir. 1984). In *N.A.A.C.P.*, the court explicitly held that facial challenges alleging overbreadth allow "courts to ignore the prudential rule that a litigant has standing to vindicate only his own constitutional rights," because such a challenge asserts that the statute "will chill the protected speech of third parties." *Id.* at 1352. In contrast, the court explained that a "quite different" type of facial challenge is one that seeks relief on the ground that the statute is unconstitutional because it "restricts protected activity in every conceivable application." *Id., quoting Munson*, 467 U.S. at 964, 104 S. Ct. 2839. In the latter case, "[b]ecause the plaintiff asserts his own injury as the basis for judicial relief . . . the court can entertain his claim without departing from traditional standing concerns." *Id.* Thus, under *N.A.A.C.P.*, a facial challenge attacking a statute in "every conceivable application" is subject to the same traditional standing requirements applied to as-applied challenges.

In both their facial and their as-applied challenge, then, in order to establish standing, Plaintiffs must allege first that they have "an intention to engage in a course of conduct arguably affected with a constitutional interest, but proscribed by a statute," and second, that "there exists a credible threat of prosecution." *Babbitt* v. *United Farm Workers Nat'l Union*, 442 U.S. 289, 298, 99 S. Ct. 2301, 60 L. Ed. 2d 895 (1979). Because Plaintiffs have so alleged, as Defendants do not dispute, they are entitled to challenge § 353a both facially and as applied to them. *See also Foti*, 146 F.3d at 635 (concluding that "[i]nadequate evidence of the

City's alleged discriminatory enforcement of the ordinance does not defeat their as-applied challenge").

While Plaintiffs do have standing to bring either type of challenge to § 353a, however, there is no substantive distinction in this case between Plaintiffs' two challenges, as Plaintiffs have not identified any unusual application of § 353a to their specific circumstances. On the contrary, they appear to lodge a broad challenge to the constitutionality of the general application of § 353a:

> Plaintiffs, both in writing and orally, have advertised, promoted, and solicited their compounded drugs for a long time prior to the enactment of Section 353a. Plaintiffs intend and need to continue to advertise, promote and solicit compounded drugs. Moreover, while the FDA argues that it has not "applied or enforced [Section 353a] against plaintiffs or any other individual or group" . . ., the FDA has "not indicated that [it] will not enforce the advertisement ban found in [§ 353a]."

Thus, Plaintiffs simply present themselves as typical parties who may be harmed by the application of § 353a. Thus, Plaintiffs' as-applied challenge is subsumed by their facial challenge, and any conclusion by this court that § 353a is unconstitutional as applied to Plaintiffs would also entail the conclusion that § 353a is unconstitutional "in every conceivable application." *See also Gaudiya Vaishnava Society*, 7 F. Supp. 2d at 1043 n.6 (concluding that where the plaintiff "failed to offer any evidence that the . . . Ordinance is unconstitutional in the manner in which it was applied to [the plaintiff's] particular speech activity, a necessary element of an as-applied challenge," the court's conclusions with respect to the plaintiff's facial and as-applied challenges apply with equal force to both arguments).

B. *Constitutionality of § 353a*

Plaintiffs challenge two subsections of § 353a. The first of these is contained in 353a(a), which requires that a prescription for the particular compounded drug be unsolicited and that it be prepared for an identified patient. That section provides:

> Sections 351(A)(2)(B), 352(f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the *unsolicited* receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient.

(emphasis added). Subsection (c) of § 353a imposes a similar condition on the exemption, prohibiting any advertising and promotion of particular compounded drugs:

> A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician *does not advertise or promote the* compounding of any *particular drug, class of drug, or type of drug.* The pharmacy, licensed pharmacist, or licensed physician *may advertise and promote* the compounding *service* provided by the licensed pharmacist or licensed physician.

21 U.S.C. § 353a(c) (emphasis added). Taken together, subsections (a) and (c) of § 353a establish that pharmacists may compound drugs without being subject to the requirements of the Act, if 1) the compounded drug is prepared for an individual patient in response to an unsolicited prescription from a physician, and 2) the

pharmacist refrains from advertising or promoting the compounding of particular drugs.

Plaintiffs argue § 353a(a) and (c) impermissibly infringe on protected rights under the First Amendment. The parties agree that the speech implicated by these sections is limited to commercial speech, and the applicable test is therefore that set forth in *Central Hudson.* Such speech represents "expression related solely to the economic interests of the speaker and its audience," *see Central Hudson Gas & Electric Corp.* v. *Pub. Service Comm'n of New York*, 447 U.S. 557, 561, 100 S. Ct. 2343, 65 L. Ed. 2d 341 (1980), and "does no more than propose a commercial transaction." *Virginia State Bd. of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 752, 96 S. Ct. 1817, 48 L. Ed. 2d 346 (1976).

It is well-settled that "[t]he First Amendment . . . protects commercial speech from unwarranted governmental regulation." *Valley Broadcasting Co.* v. *United States*, 107 F.3d 1328, 1330 (9th Cir.1997) (*citing Central Hudson*, 447 U.S. at 561-62, 100 S. Ct. 2343). However, "[i]f commercial speech only is threatened, the requirements of the First Amendment are less rigorous." *Washington Mercantile*, 733 F.2d at 689. "The law has developed to ensure that advertising provides consumers with accurate information about the availability of goods and services." *44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484, 496, 116 S. Ct. 1495, 134 L. Ed. 2d 711 (1996). Consistent with this ideal, courts have encouraged and protected commercial speech, but have limited that protection to "the dissemination of truthful and nonmisleading commercial messages about lawful products and services." *Id.* (*citing* Kozinski & Banner, *The Anti-History and Pre-History of Commercial Speech*, 71 Tex. L. Rev. 747 (1993)).

In *Central Hudson*, the Supreme Court articulated the applicable test to evaluate the constitutionality of government regulations limiting commercial speech. The four-part *Central Hudson* test reflects a "more relaxed inquiry" than that applied to restrictions of non-commercial speech. *Ass'n of Nat'l Advertisers, Inc.* v. *Lungren*, 44 F.3d 726, 728-29 (9th Cir. 1994). The test provides:

> At the outset, we must determine whether the expression is protected by the First Amendment. For commercial speech to come within that provision, it at least must concern lawful activity and not be misleading. Next, we ask whether the asserted governmental interest is substantial. If both inquiries yield positive answers, we must determine whether the regulation directly advances the governmental interest asserted, and whether it is not more extensive than is necessary to serve that interest.

Id. at 566, 100 S. Ct. 2343. "Under this intermediate scrutiny, the asserted governmental interest must be 'substantial,' rather than 'compelling,' and the regulation adopted must 'directly advance' this interest, rather than be 'precisely drawn.'" *Lungren*, 44 F.3d at 729 (*citing Central Hudson*, 447 U.S. at 566, 100 S. Ct. 2343).

The Central Hudson test can be distilled into four discrete questions: 1) As a threshold matter, is the targeted speech constitutionally protected; 2) has the Government asserted a "substantial" governmental interest; 3) does the regulation "directly advance" the

asserted interest; and 4) is the restriction more extensive than necessary to achieve the asserted governmental interest. If factor (1) is answered in the affirmative, the court must proceed to an analysis of the three remaining factors to determine whether the statute is justified by the asserted governmental interest it purportedly serves.

1. *Is the Speech Targeted by § 353a Constitutionally Protected?*

The first factor of the *Central Hudson* test directs the court to analyze whether, as a threshold matter, the speech in question is protected by the First Amendment. Under *Central Hudson*, "for commercial speech to come within that provision, it must at least concern lawful activity and not be misleading." 447 U.S. at 566, 100 S. Ct. 2343.

In this case, Defendants do not argue that the restrictions at issue involve illegal activity; rather, they contend that the targeted speech is misleading and may be restricted on that basis. Courts have divided the "misleading" element of the *Central Hudson* test into two categories: "inherently" misleading and "potentially" misleading. If speech is "inherently" misleading, it may be restricted without reference to the remaining three *Central Hudson* factors. To evaluate whether speech is "inherently misleading," courts will consider whether the speech is "more likely to deceive the public than to inform it," *Central Hudson*, 447 U.S. at 563, 100 S. Ct. 2343; whether there are substantial "possibilities for deception," *Friedman*, 440 U.S. at 13, 99 S. Ct. 887; whether experience has shown that such advertising is subject to abuse, *In re R.M.J.*, 455 U.S. 191, 203, 102 S. Ct. 929, 71 L. Ed. 2d 64 (1982); and whether the intended audience has the ability to

evaluate the claims made. *Id.* Because inherently misleading speech carries substantial social harms, and the state obviously has a compelling interest in preventing such harms, speech that is inherently misleading may be regulated on that basis alone. *See In re R.M.J.*, 455 U.S. at 203, 102 S. Ct. 929.

If speech is merely "potentially" misleading, however, it may not be proscribed under the commercial speech test without analysis under the remaining three factors. "If the protections afforded commercial speech are to retain their force we cannot allow rote invocation of the words potentially misleading to supplant [the government's burden]." *Ibanez* v. *Florida Dep't of Bus. and Prof'l Regulation*, 512 U.S. 136, 146, 114 S. Ct. 2084, 129 L. Ed. 2d 118 (1994) (internal citations and quotation marks omitted). Where the speech may or may not be misleading in any given case, it is only "potentially" misleading, and may not be subject to a blanket prohibition. *Lungren*, 44 F.3d at 731-32. In such cases, courts should evaluate a speech restriction "focusing on its potential for deception in light of the lessons of experience and the nature of the target audience." *Id.* at 732.

Here, Defendants contend that the speech at issue is inherently misleading, and thus may be prohibited without regard to the remaining *Central Hudson* factors. In the alternative, they argue that the speech is at least potentially misleading, and that the Government is therefore allowed greater deference in its regulation.

Defendants first argue that "[b]y their very nature," advertisements for compounded drugs "make express and implicit statements" about the safety and effectiveness of such drugs. They further claim that

"[b]ecause compounded drugs have not been shown to be safe and effective under the Act's longstanding and universally recognized scientific standards, advertisements, promotions, and solicitations involving particular unapproved compounded drugs are inherently misleading because they suggest that these unapproved drugs have therapeutic value."

Two considerations counsel the court to conclude that the speech targeted by the restrictions at issue is not "inherently misleading." First, there is no evidence in this case that the prohibited statements contain any information that is actually false. On the contrary, Plaintiffs seek to provide truthful information about their compounding services, the various compounded drugs they produce, and in some cases, research materials on the safety and effectiveness of the particular compounded drug. There is no false information in any of Plaintiffs' promotions, a fact that Defendants do not dispute. Defendants' unsupported assertion that the public will be misled into believing, by implication alone, that compounded drugs have passed FDA tests and been approved, is insufficient to warrant the conclusion that the restricted speech is "inherently misleading."

Defendants' own statement illustrates that the speech at issue is not inherently misleading. Defendants assert that the targeted speech is inherently misleading "because they suggest that these unapproved drugs have therapeutic value." Yet Defendants themselves presumably believe that compounded drugs have therapeutic value in some cases; otherwise, they would prohibit the unapproved use of such drugs altogether. Thus, even if it is true, as Defendants argue, that the promotion of compounded drugs suggests that they

have therapeutic value, according to Defendants' own argument, this is frequently an accurate and truthful claim about the drug's benefits.

Defendants rely on *United States* v. *An Article . . . Acu-Dot*, 483 F. Supp. 1311, 1315 (N.D. Ohio 1980) for the proposition that advertisements of unapproved drugs, such as the compounded drugs at issue here, are inherently misleading because they falsely indicate that the drugs have obtained FDA approval and that the drugs are therefore safe and effective. Defendants' reliance on *Acu-Dot*, however, is misplaced. There, the defendants were manufacturers of a "small, pin-head sized magnet attached to the underside of a circular, adhesive patch," which was designed to work as a minor pain reliever. The defendants marketed the product as useful "[f]or temporary relief of occasional minor aches and pains of muscles and joints." 483 F. Supp. at 1312. The FDA brought suit against the defendants, claiming that the product had only a placebo effect, and therefore, the defendants' promotional statements about the product were misleading. The FDA relied on the testimony of several experts who testified that "the devices could not achieve the effect alleged by the labeling, other than through a placebo effect." 483 F. Supp. at 1313. The defendants apparently did not dispute that the drugs had only a placebo effect, but contended that the placebo effect was sufficient to warrant the defendants' claims regarding the drugs' health benefits.

The court disagreed. The court emphasized that the device itself could not provide the benefits claimed in the advertisement; all physical benefits enjoyed by its users stemmed from a mental response to using the device. The court concluded that "the device often can

achieve its claims of providing 'temporary relief of occasional minor aches and pains of muscles and joints'; but this effect is the result of nothing more than sophisticated marketing chicanery." 483 F. Supp. at 1314. On these facts, the court held that the marketer's claim that the device itself provided temporary relief of minor aches and pains was false, and thus also "misleading."

Here, there is neither evidence nor argument that Plaintiffs will attribute therapeutic benefits to their products that the products themselves are unable to provide. Defendants simply assert that their promotions "imply," by omitting certain facts, that compounded drugs have obtained FDA approval. This assertion, without more, is clearly inadequate to warrant the conclusion that the commercial speech targeted by § 353a is "inherently misleading."

A second consideration militating against the conclusion that the speech is inherently misleading is that to the extent the targeted speech may have the potential to mislead, that misleading element can be reduced or removed altogether by the use of a narrower restriction. Were the FDA attempting to prevent the public from being misled by the implication that compounded drugs had been approved by the FDA, it could simply require pharmacists to include a disclaimer on their advertisements indicating that FDA approval had not been obtained.[7]

---

[7] A required disclaimer on each advertisement or solicitation indicating that the particular compounded drug has not been tested or approved by the FDA as safe and effective would satisfy this goal.

A plurality of the United States Supreme Court reached a similar conclusion in *Peel* v. *Attorney Registration & Disciplinary Comm'n of Ill.*, 496 U.S. 91, 110 S. Ct. 2281, 110 L. Ed. 2d 83 (1990). There, the Attorney Registration and Disciplinary Commission of Illinois brought disciplinary proceedings against the plaintiff under a rule prohibiting attorneys from representing themselves to the public as specialists. The plaintiff, an attorney, was licensed to practice law in Illinois and other states, and also had obtained a "Certificate in Civil Trial Advocacy" from the National Board of Trial Advocacy. In his letterhead, the plaintiff stated his name, which was followed by a notation that read "Certified Civil Trial Specialist By the [Board]," and another notation that read "Licensed: Illinois, Missouri, Arizona." The Commission asserted that by listing these pieces of information in this way, the plaintiff implied to the public that he was a certified legal specialist. The Illinois Supreme Court agreed, holding that the First Amendment did not protect the plaintiff's letterhead because the public could confuse the State and the Board as the sources of the plaintiff's certification and his license to practice.

The Supreme Court reversed. The Court explained that a state may prohibit inherently misleading speech entirely, but it cannot impose an absolute prohibition if the information may be presented in a non-misleading manner. The Court emphasized that "[t]he facts stated on petitioner's letterhead are true and verifiable," and that there was no contention that "any potential client or person was actually misled or deceived" by the restricted speech. The Court recommended that as an alternative to a broad prohibition, the defendants could require a disclaimer to ensure that complete infor-

mation about attorneys' qualifications was provided to the public. It could not, however, broadly proscribe truthful information whose negligible misleading content could be remedied by providing more information. *See also Virginia Bd. of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 772 n.24, 96 S. Ct. 1817, 48 L. Ed. 2d 346 (1976) (noting that the state may regulate a commercial message so that it will "appear in such a form, or include such additional information, warnings, and disclaimers, as are necessary to prevent its being deceptive"); *Nutritional Health Alliance* v. *Shalala*, 953 F. Supp. 526, 528 (S.D.N.Y. 1997) (concluding that health claims not approved by the FDA are not inherently misleading where "at least some can be presented in a non-misleading fashion").

In *Washington Legal Foundation* v. *Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998) ("*WLF*"), the court applied the same reasoning to a case involving FDA regulations. There, a public interest group sought to enjoin the enforcement of government restrictions regulating the promotion and advertisement of "off- label" uses for prescription drugs.[8] The FDA argued that statements promoting off-label uses not approved by the FDA are "inherently misleading."

The court rejected the FDA's argument, which it characterized as one claiming that "any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or misleading until

[8] "Off-label" uses involve using an FDA-approved drug for uses that have themselves not been approved, such as treating a condition not indicated on the label or treating the indicated condition but varying other factors, such as the dosing regimen.

the FDA has had the opportunity to evaluate them." 13 F. Supp. 2d at 67. It stated that the FDA "exaggerate[d] its overall place in the universe" by arguing that promotion of off-label drugs was "untruthful or inherently misleading merely because the FDA ha[d] not yet had the opportunity to evaluate the claim." 13 F. Supp. 2d at 67. The court concluded that the targeted statements about off-label uses were not "inherently misleading," because "at least some can be presented in a non-misleading fashion." *Id.* (*quoting Nutritional Health Alliance* v. *Shalala*, 953 F. Supp. 526, 528 (S.D.N.Y. 1997)).

As indicated earlier, if the FDA believed that the targeted statements in this case were likely to mislead, it could simply require that pharmacists compounding drugs include disclaimers in their advertisements, clarifying that the compounded drug had not passed the FDA approval process required of new drugs. In doing so, any potential the targeted speech may have to mislead the public would be prevented, with no violence done to free speech. The availability of such a reasonable alternative restriction militates against the conclusion that the speech at issue is "inherently misleading."

The court therefore concludes that the speech at issue in this case is not inherently misleading, and thus may not be prohibited without reference to the remaining *Central Hudson* factors. The court recognizes, however, that the targeted promotional statements have the potential to mislead, because consumers may, under certain circumstances, believe that the drugs have survived the rigorous testing and labeling requirements imposed on new drugs. "[T]he government may have more leeway" in restricting commercial speech

when there is the potential to mislead on issues involving public health. *Pearson* v. *Shalala*, 164 F.3d 650, 659 (D.C. Cir. 1999). However, "it must still meet its burden of justifying a restriction on speech." *Id.* If there is any likelihood that "truthful and nonmisleading expression will be snared along with . . . deceptive commercial speech, the State must satisfy the remainder of the Central Hudson test by demonstrating that its restriction serves a substantial state interest and is designed in a reasonable way to accomplish that end." *Id.* at 768-69. Thus, the court must proceed to an analysis of the remaining factors to evaluate the constitutionality of § 353a, cognizant of the fact that the speech targeted by the restrictions are "potentially misleading," and "focusing on its potential for deception in light of the lessons of experience and the nature of the target audience." *Lungren*, 44 F.3d at 732.

2. *Does the Government assert a Substantial Government Interest?*

In this case, Defendants allege that three substantial interests are served by § 353a. First, Defendants point to the general goal of protecting the public health and safety. Plaintiffs do not dispute, as they cannot, that this is a substantial government interest entitled to federal protection. The Supreme Court has clearly stated that "the Government has a significant interest in protecting the health, safety, and welfare of its citizens." *Rubin*, 514 U.S. at 485, 115 S. Ct. 1585. Thus, the court agrees with Defendants that its goal of serving the public health and safety meet the substantial government interest request.

Defendants also assert two more specific goals allegedly advanced by the statute. Defendants contend first that § 353a serves the goal of maintaining the

integrity of the drug approval process. The court agrees that this interest is substantial. Congress has declared that all new drugs must be tested and approved by the FDA. The purpose of this requirement is to ensure that new drugs introduced into the market meet basic standards of safety and effectiveness. The FDA's approval gives consumers important information to evaluate a particular drug, and the integrity of this process is clearly necessary to its effectiveness and reliability. *See also WLF*, 13 F. Supp. 2d at 71 (concluding that encouraging manufacturers of approved drugs to subject off-label uses to the drug approval process is a substantial governmental interest).

Finally, Defendants argue that they have a substantial interest in balancing "the continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." Defendants' Motion at 20. The Supreme Court has confirmed that the government's effort to balance competing goals may be a substantial interest worthy of governmental protection. *See United States* v. *Edge Broadcasting Co.*, 509 U.S. 418, 428, 113 S. Ct. 2696, 125 L. Ed. 2d 345 (1993) ("Edge") (concluding that the "congressional policy of balancing the interests of lottery and nonlottery States is the substantial governmental interest that satisfies *Central Hudson*"). However, a finding that Defendants' asserted interest in balancing its competing goals requires a finding by this court that the competing goals themselves are substantial.

With respect to the first of these competing goals, Plaintiffs themselves echo Defendants' claim that individual patients may benefit from the compounding

of particular drugs to accommodate unique needs, such as age differences, allergies or unusual dosages. The court therefore agrees that the government has a substantial interest in ensuring the continued availability of compounded drugs for use by individual patients.

The court is not convinced, however, that Defendants have a substantial interest in preventing "compounding under the guise of manufacturing." Defendants have offered no definition of either manufacturing or compounding, apparently because the Modernization Act itself offers no such definition. Thus, there is no coherent way for this court to determine whether Defendants have a substantial interest in encouraging one while limiting the other. In their argument, Defendants appear to equate high volume distribution with manufacturing and low volume distribution with compounding. In their Motion, they insist that they must "limit the volume of compounding because of the increased health risks associated with a large number of patients receiving drugs that are not subject to the same quality control standards that apply to ordinary manufactured drugs." Defendants' Motion at 21. This framework, however, obviously cannot support Defendants' asserted interest in preventing compounding allegedly done under the guise of manufacturing. First, it does nothing to clarify the difference between manufacturing and compounding. Furthermore, even were the distinction clear, this argument neither explains nor supports the contention that there are "increased health risks associated with a large number of patients" receiving compounded drugs, but that compounded drugs in small quantities produce an overall benefit to the public health.

If, on the other hand, Defendants believe that the relevant distinction is between those drugs that are FDA approved and those that are not, the court agrees that the FDA has a legitimate interest in preventing pharmacists from circumventing FDA requirements by changing the description of their products. To the extent this is the basis for Defendants' distinction, the court agrees that it is substantial. The problem with this argument is that without more, it ultimately reduces to equating manufacturing with approved drugs and compounding with unapproved drugs. At that point, any interest Defendants assert in making compounded drugs available to individual patients is no longer tenable. Therefore, on the facts before it, the court is unable to either identify or acknowledge the significance of the distinction between manufactured and compounded drugs.[9] For this reason, it cannot agree with Defendants that the Government has a

---

[9] In reality, the practical difference in this case between Defendants' notion of manufacturing and compounding may actually be embodied by the precise issue the court must address in this order. Specifically, it appears that Defendants would label pharmacy-initiated drug combining as manufacturing, and patient- or physician-initiated drug combining as compounding. This frames the distinction by looking to whether the pharmacist or other drug producer advertised, promoted or otherwise initiated the sale and use of the particular drug product. Of course, to accept Defendants' distinction, and more importantly, to accept that Defendants have a substantial interest in preserving this distinction, is to agree that Defendants have a substantial interest in preventing pharmacists from advertising or promoting particular compounded drugs, because to allow such promotion would be to allow pharmacists to manufacture under the guise of compounding. This conclusion begs the question before the court, which is whether the speech restrictions contained in § 353a are legitimate.

substantial interest in achieving the imprecise and undefined balance it purportedly seeks here.

The court thus concludes that Defendants' asserted interests of protecting the public health and safety and preserving the integrity of the FDA approval process are substantial and worthy of protection under *Central Hudson*. However, Defendants third asserted interest of balancing the need for compounded drugs in individual cases against the goal of preventing manufacturing under the guise of compounding is insufficiently clear in this case to constitute a substantial governmental interest. For these reasons, whether § 353a withstands constitutional scrutiny turns on whether 1) it directly advances the government's goals of protecting the public health and welfare, and preserving the integrity of the FDA drug approval process, and 2) it is narrowly tailored to accomplish these goals.

3. *Does the Regulation "Directly Advance" the Governmental Interests Asserted?*

Under the third factor, the court examines whether the regulation at issue "directly advance[s] the state interest involved." *Central Hudson*, 100 S. Ct. at 2350. Under this test, "the regulation may not be sustained if it provides only ineffective or remote support for the government's purpose." *Id.* Rather, to satisfy this requirement, "the government must demonstrate that 'its restrictions will in fact alleviate [the asserted harms] to a material degree.'" *Valley Broadcasting Co.* v. *United States*, 107 F.3d 1328, 1334 (9th Cir. 1997) (*quoting Edenfield* v. *Fane*, 507 U.S. 761, 769, 113 S. Ct. 1792, 123 L. Ed. 2d 543 (1993)).

In *Edenfeld*, the Supreme Court clarified that once the first two factors have been satisfied, the Government carries the burden of demonstrating that the challenged regulation advances the Government's interest "in a direct and material way." 507 U.S. at 767, 113 S. Ct. 1792. That burden "is not satisfied by mere speculation or conjecture; rather, a governmental body seeking to sustain a restriction on commercial speech must demonstrate that the harms it recites are real and that its restriction will in fact alleviate them to a material degree." *Id.* at 770-771, 113 S. Ct. 1792.

To satisfy this burden, Defendants advance the following argument: "The advertising restrictions in subsections (a) and (c) 'are intended to ensure that the volume of compounding does not approach that ordinarily associated with drug manufacturing.'" Defendants' Motion at 22 (*quoting* 143 Cong. Rec. S9840 (statement of Senator Kennedy)). Thus, at bottom, Defendants assert that the speech-related restrictions in § 353a are necessary to limit the volume of compounded drugs, thereby ostensibly protecting the public against the purported health risks associated with compounded drugs.

Defendants' argument fails to draw the necessary connection between their asserted interests on the one hand, and restricting the volume of compounded drugs on the other. Defendants concede that all compounded drugs must be prescribed by a physician, and they even encourage the use of compounded drugs for individual patients when the drugs are requested by a physician or patient. Thus, Defendants freely admit that making compounded drugs available in some number represents an overall benefit to the public health. However, as soon as the sale of the drug is encouraged by the pharmacist, Defendants insist that it poses a danger to the public health that warrants restriction.

The D.C. Circuit rejected an argument similar to Defendants' in *Pearson* v. *Shalala*, 164 F.3d 650 (D.C. Cir. 1999). There, similar to the FDA's argument here, the FDA claimed that the public health would be advanced by prohibiting drug producers from making health claims about FDA-approved dietary supplements, where the health claims themselves had not been approved by the FDA. Rejecting the FDA's argument, the court stated:

> The government simply asserts its 'common sense judgment' that the health of consumers is advanced directly by barring any health claims not approved by the FDA. Because it is not claimed that the product is harmful, the government's underlying—if unarticulated—premise must be that consumers have a limited amount of either attention or dollars that could be devoted to pursuing health through nutrition, and therefore products that are not indisputably health enhancing should be discouraged as threatening to crowd out more worthy expenditures. We are rather dubious that this simplistic view of human nature or market behavior is sound, but, in any event, it surely cannot be said that this notion—which the government does not even dare openly to set forth—is a direct pursuit of consumer health; it would seem a rather indirect route, to say the least.

Similar to the defendants in *Pearson*, Defendants in this case have not claimed that compounded drugs, in and of themselves, are harmful. Quite the contrary, they assert a "substantial interest" in ensuring the availability of such drugs in limited quantities. Instead, Defendants assert that the *volume* of compounded

drugs must be controlled to protect the public safety, with no argument as to why compounded drugs in greater quantity pose a higher risk to public safety.[10] Apparently, Defendants believe that as the volume of compounded drugs increases, the balance shifts, so that the benefits of compounded drugs are outweighed by their costs. Defendants have produced no evidence that such a phenomenon is likely to occur.

The only argument put forth by Defendants that may support this implicit claim is their unsupported assertion that physicians and consumers are unable to evaluate the health claims about compounded drugs made by advertising pharmacists. Defendants concede that Plaintiffs regularly include research and studies in their promotional materials, but boldly insist nonetheless that "most practicing physicians do not have the time or the training to make independent assessments . . . and reach an independent, objective conclusion as to the benefits, risks, safety and effectiveness of a particular compounded drug that has not undergone the approval process."

Several courts have considered and flatly dismissed Defendants' argument, rejecting the "paternalistic" view that suppression of truthful speech is necessary to protect physicians and consumers from their own misuse of truthful information. In *WLF*, for example, the court faced the similar question of whether the state could prohibit pharmacists from promoting off-label uses of approved drugs. The court rejected the government's assertion that a prohibition was neces-

---

[10] It must be kept in mind that all dispensing of compounded drugs must be under a valid prescription to an individual patient by a licensed physician.

sary to prevent the misuse of drugs by physicians. It reasoned that "despite the FDA's occasional statements in its briefs to the contrary, physicians are a highly educated, professionally-trained and sophisticated audience. In making prescribing decisions, doctors want (and need) to know first and foremost if the drug is the most safe and effective means to treat the conditions suffered by the patients." *WLF*, 13 F. Supp. 2d at 63. *See also 44 Liquormart*, 517 U.S. at 503, 116 S. Ct. 1495 (recognizing that "[t]he First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good").

Perhaps the most insightful rendering of this principle is that reflected in the Supreme Court's decision in *Virginia Bd. of Pharmacy*. There, the court struck down a Virginia statute prohibiting pharmacists from advertising their prices for prescription drugs. In reaching its conclusion, the court expressed its aversion to the use of suppression as a means to prevent "uninformed" individuals from misusing accurate information. The Court explained:

> There is, of course, an alternative to this highly paternalistic approach. That alternative is to assume that this information is not in itself harmful, that people will perceive their own best interests if only they are well enough informed, and that the best means to that end is to open the channels of communication rather than to close them. If they are truly open, nothing prevents a "professional" pharmacist from marketing his own assertedly superior product, and contrasting it with that of the low-cost, high-volume prescription drug retailer. But the choice among these alternative approaches is not

> ours to make or the Virginia General Assembly's. It is precisely this kind of choice, between the dangers of suppressing information, and the dangers of its misuse if it is freely available, that the First Amendment makes for us.

Id. at 770, 96 S. Ct. 1817.

The court agrees that suppression of truthful and accurate information as a means to protect society from its own misuse is anathema to the principles of the First Amendment. Were the FDA concerned with serving public health by preventing the purported harms of compounded drugs, it could certainly find a more direct route to that end than traveling through the protected area of speech. There is no evidence on the record that reducing the volume of compounded drugs will serve public health, and even if such evidence existed, broad prohibitions on truthful and accurate speech is an illegitimate method of achieving this goal.

Nor does § 353a directly advance the goal of preserving the integrity of the FDA approval process. If the FDA were concerned with ensuring that drug producers not avoid FDA regulations, it could easily require that all drugs, including compounded drugs, obtain FDA approval before being introduced into the stream of commerce. This would certainly be a more "direct" route to maintaining the integrity of the approval process. In actuality, there appears to be no logical connection between the regulation of speech on the one hand and the preservation of the integrity of the FDA's drug approval process on the other. The remaining sections of § 353a, which regulate the ingredients that may be used and limit the total amount of compounded drugs that may be distributed, would seem to more directly achieve those goals.

Furthermore, even if § 353a did not suffer from these flaws, given the substantial exceptions to its application that dramatically limit its reach, this court cannot conclude that § 353a directly advances the FDA's asserted interests. Pharmacists are free to advertise compounded *services*, as long as they do not advertise "any particular drug, class of drug, or type of drug." Thus, a pharmacy may advertise its compounding experience, including promotional activities at educational, professional and trade meetings, likely increasing the overall volume of compounded drugs, as long as it does not promote the compounding of any particular drug or class of drugs.

Section 353a also does not prohibit consultations between the compounding pharmacist and patients or physicians. By its terms, § 353a specifically allows a compounded drug to be based on either an unsolicited prescription or "a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. § 353a(a). The provision permits a pharmacist to call a physician, after a patient has presented a prescription that indicates a compounded product may be desirable, to discuss the possibility of prescribing a compounded product. Thus, the statutory scheme essentially bars pharmacists from promoting particular drugs, but leaves them free to either advertise compounding services generally or initiate discussions with physicians or patients regarding particular compounded products needed by individual patients. It is difficult to see how the communication of the same information can both serve and undermine the public health, depending on which party initiates the contact or the method used to communicate it.

Finally, if Defendants are concerned with limiting the volume of compounded drugs, as they allege, § 353a(b)(3) would appear to undermine that goal, because it explicitly permits compounded drugs to constitute up to 5% of interstate drug distributions, and 100% of intrastate drug distributions. Moreover, if a pharmacist has a Memorandum of Understanding ("MOU") with the Secretary of Health and Human Services, it can distribute as much as 20% of its total interstate drug distributions in the form of compounded drugs. For a large pharmacy such as Payless or Walgreens, this would permit the distribution of compounded drugs in substantial numbers, amounting to sales in the millions of dollars.

In *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 115 S. Ct. 1585, 131 L. Ed. 2d 532 (1995), the court relied on similar considerations to strike down a federal restriction on alcohol advertising, reasoning that there was "little chance" the restriction could advance the government's asserted goal, where "other provisions of the same Act directly undermine[d] and counteract[ed] its effects." 514 U.S. at 489, 115 S. Ct. 1585. In the Supreme Court's recent decision in *Greater New Orleans Broadcasting Ass'n* v. *United States*, 527 U.S. 173, 119 S. Ct. 1923, 144 L. Ed. 2d 161 (1999), the Court reached the same conclusion. There, the Court struck down a federal ban on gambling advertising, in part, because its application was riddled with exceptions, making it ineffective in serving its purported purpose. The Court explained that "[t]he operation of § 1304 and its attendant regulatory regime is so pierced by exemptions and inconsistencies that the Government cannot hope to exonerate it." 527 U.S. at ——, 119 S. Ct. at 1925. Similarly, in this case, Defendants' primary

purpose for § 353a—limiting the volume of compounded drugs in order to serve the public health—is undercut by the exceptions allowed in its own provisions. Under these circumstances, § 353a does not "directly advance" Defendants' asserted interests.

The court therefore finds that the speech-related restrictions contained in § 353a do not directly advance the Government's asserted interests, as required by the third *Central Hudson* factor. However, even were the court to conclude that the statute could satisfy this requirement, § 353a is also flawed because it fails the fourth factor of the *Central Hudson*, in that it is not narrowly tailored to achieve its stated purposes.

4. *Is the Speech Restriction more Extensive than Necessary to Serve the Interests that Support it?*

Under the fourth *Central Hudson* factor, the court must consider whether the restriction is "more extensive than is necessary to serve [the asserted state] interest." *Central Hudson*, 447 U.S. at 566, 100 S. Ct. 2343. "The fourth part of the test complements the direct-advancement inquiry of the third, asking whether the speech restriction is not more extensive than necessary to serve the interests that support it." *Greater New Orleans*, 527 U.S. at ——, 119 S. Ct. at 1932.

Nearly twenty years after *Central Hudson* was decided, in the face of a disagreement over the appropriate interpretation of the fourth *Central Hudson* factor, the Supreme Court revisited the issue in *Bd. of Trustees of the State Univ. of New York* v. *Fox*, 492 U.S. 469, 109 S. Ct. 3028, 106 L. Ed. 2d 388 (1989). In *Fox*, the Court explained that contrary to the holdings of several circuits, the fourth factor does not require

that a restriction be "absolutely the least severe that will achieve the desired end." Rather, what is required is a

> 'fit' between the legislature's ends and the means chosen to accomplish those ends—a fit that is not necessarily perfect, but reasonable; that represents not necessarily the single best disposition but one whose scope is in proportion to the ends served; that employs not necessarily the least restrictive means but . . . a means narrowly tailored to achieve the desired objective.

Fox, 492 U.S. at 480, 109 S. Ct. 3028 (*quoting Posadas de Puerto Rico Assoc.* v. *Tourism Co. of Puerto Rico*, 478 U.S. 328, 341, 106 S. Ct. 2968, 92 L. Ed. 2d 266 (1986)). While giving more deference to the state, the *Fox* Court noted at the same time that restrictions previously struck down under the *Central Hudson* test were usually "substantially excessive, disregarding 'far less restrictive and more precise means.'" *Fox*, 492 U.S. at 479, 109 S. Ct. 3028.

The Ninth Circuit subsequently considered the implication of *Fox* in *Project 80's, Inc.* v. *City of Pocatello*, 942 F.2d 635, 637 (9th Cir. 1991). Interpreting the *Fox* Court's holding, the Ninth Circuit stated that in order to find a "reasonable fit" between the state regulation and its asserted interest, the court must conclude that the regulation is "narrowly tailored to serve substantial governmental interests." *Project 80's*, 942 F.2d at 637. The court reasoned:

> By pointing out the alternatives available to the cities to advance their interests, we do not impose a least restrictive means requirement. Rather, we conclude, as did the Supreme Court in Fox [*sic*],

> that restrictions which disregard far less restrictive and more precise means are not narrowly tailored.

942 F.2d at 638. Thus, where there are "far less restrictive and more precise means" that will achieve the desire end, the fourth factor under *Central Hudson* is not satisfied. *Id.*; *see also Cal-Almond, Inc.* v. *United States Dep't of Agriculture*, 14 F.3d 429, 440 (9th Cir. 1993) (striking down advertising regulations that were "more extensive than necessary to serve the interest" asserted).

Applying this test to the instant case, it is clear that § 353a is not "narrowly tailored." As previously noted, were the FDA merely concerned with protecting the public from being misled about whether a drug has been FDA approved, it could require disclaimers to prevent any potential for confusion. The disclaimers could specifically state that the compounded drugs being advertised had not been subjected to the FDA's drug approval process. Included in these disclaimers could be statements about the costs and benefits of compounded drugs. The FDA could even require pharmacists to indicate that compounded drugs are intended for the specific needs of individual patients that cannot be met with approved manufactured drug products.

In *Pearson*, the court held that the FDA was required to consider disclaimers as an alternative to an outright ban on advertising. The court reviewed several recent Supreme Court cases "repeatedly pointing to disclaimers as constitutionally preferable to outright suppression." 164 F.3d at 657; *see Peel*, 496 U.S. at 110, 110 S. Ct. 2281; *R.M.J.*, 455 U.S. at 206 n.20, 102 S. Ct. 929; *Shapero* v. *Kentucky Bar Ass'n.*, 486 U.S. 466, 478, 108 S. Ct. 1916, 100 L. Ed. 2d 475 (1988). The court concluded that where a statute

prohibits "incomplete" advertising, "the preferred remedy is more disclosure, rather than less." *Id.*, (*citing Bates* v. *State Bar of Arizona*, 433 U.S. 350, 376, 97 S. Ct. 2691, 53 L. Ed. 2d 810 (1977)). Here, too, Defendants could require disclaimers as an alternative to their prohibition on advertising compounded drugs, which would clearly represent a far less restrictive means to accomplish the FDA's asserted goals.

Alternatively, if Defendants' intention is to protect the public health and welfare and to preserve the integrity of the FDA approval process, and they believe that compounded drugs threaten these concerns, they could subject compounded drugs to the safety testing imposed on new drugs. While this would of course represent a broader restriction on the production of compounded drugs, it would not threaten the free speech interests implicated by § 353a.

Courts have repeatedly held that where the benefits reaped by restrictions on speech could be obtained through nonspeech restrictions, speech restrictions should be viewed with great suspicion. *See, e.g.*, *Greater New Orleans*, 527 U.S. at ——-——, 119 S. Ct. at 1934-35 ("It is well settled that the First Amendment mandates closer scrutiny of government restrictions on speech than of its regulation of commerce alone"); *see also 44 Liquormart*, 517 U.S. at 500, 116 S. Ct. 1495 (recognizing that "special concerns arise from regulations that entirely suppress commercial speech in order to pursue a nonspeech-related policy"). In its recent decision in *Greater New Orleans*, the Court recognized the harms of restrictions that indiscriminately and unnecessarily capture innocent speech. The Court there held that the statute at issue was suspect because it "sacrifice[d] an intolerable amount of truthful speech

about lawful conduct when compared to all of the policies at stake and the social ills that one could reasonably hope such a ban to eliminate." *Id.*

Thus, even were Defendants able to show that compounded drugs carry substantial health risks, and therefore that their volume should be limited, the proper remedy to such a problem is not broad prohibitions on truthful speech. The *Greater New Orleans* Court reminds us that "the power to prohibit or to regulate particular conduct does not necessarily include the power to prohibit or regulate speech about that conduct." 527 U.S. at ——, 119 S. Ct. at 1934 (citation omitted). In this case, there is no question that Congress has the authority, indeed the responsibility, to regulate the availability of potentially dangerous drugs. Where such an end can be achieved without reliance on speech restrictions, however, Congress cannot, consistent with the First Amendment, use protected speech to accomplish its task. As the Court in *44 Liquormart* recognized, "[t]he First Amendment makes clear that the Constitution presumes that attempts to regulate speech are more dangerous than attempts to regulate conduct." 517 U.S. at 511, 116 S. Ct. 1495.

In sum, by enacting § 353a, Defendants have impermissibly infringed on protected speech to advance interests that can be served through far less restrictive means. While Defendants have identified substantial government interests they seek to serve, § 353a does not directly advance these interests and is clearly not narrowly tailored to accomplish its purported goals. While the Government is given more deference in its regulation of commercial speech, this deference does not override the protections of the First Amendment, which prevent the unnecessary prohibition of truthful

speech to achieve goals that may be served without implicating protected freedoms.

C. *Severability*

Having concluded that the speech-related portions of §§ 353a(a) and (c) are unconstitutional, the court must now turn to the question of whether these sections may be severed from § 353a. It is well-settled that "a court should refrain from invalidating more of the statute then is necessary." *Alaska Airlines, Inc.* v. *Brock*, 480 U.S. 678, 684, 107 S. Ct. 1476, 94 L. Ed. 2d 661 (1987) (*quoting Regan* v. *Time, Inc.*, 468 U.S. 641, 104 S. Ct. 3262, 82 L. Ed. 2d 487 (1984)). "Whenever an act of Congress contains unobjectionable provisions separable from those found to be unconstitutional, it is the duty of this court to so declare, and to maintain the act in so far as it is valid." *Regan*, 468 U.S. at 652, 104 S. Ct. 3262 (citations omitted).

Consistent with these principles, the Supreme Court has stated that if the constitutionally permissible portions of a statute are "fully operative as a law," the offending portions should be severed "[u]nless it is evident that the Legislature would not have enacted those provisions which are within its power, independently of that which is not." *Immigration & Naturalization Service* v. *Chadha*, 462 U.S. 919, 931, 103 S. Ct. 2764, 77 L. Ed. 2d 317 (1983) (*quoting Buckley* v. *Valeo*, 424 U.S. 1, 108, 96 S. Ct. 612, 46 L. Ed. 2d 659 (1976)). Thus, only if the remainder of the statute is unable to operate independently as law, or it is clear that Congress would not have enacted the statute but for the impermissible portions, may the court invalidate the entire statute.

In this case, there is no question that the offending portions of subsections (a) and (c) can be severed from the remainder of § 353a. First, while extracting the speech-related provisions will certainly reduce the reach of § 353a, this modification will not render the statute unable to operate as law. The remaining portions of § 353a substantially limit and regulate pharmacists' production and distribution of compounded drugs. Subsection (b), for example, contains numerous requirements relating to the quality of the drug's ingredients and their effectiveness in compounding. Section 353a(b)(1)(A) requires that compounded drugs consist of drugs found on a list of "bulk drug substances," as defined in the Code of Federal Regulations. Section 353a(b)(1)(C) prohibits compounding of any drug ingredients that have been deemed unsafe or ineffective. Section 353a(b)(1)(D) prevents an individual from compounding "inordinate amounts [of] any drug products that are essentially copies of a commercially available drug product." Finally, § 353a(b)(3) limits pharmacists' distribution of compounded drugs to no more than 5%, or in some cases up to 20%, of the pharmacists' total interstate distribution of prescription orders. These remaining sections clearly represent independent requirements for the production of compounded drugs, allowing § 353a to be "fully operative as a law" even in the absence of the offending speech-related sections.

Furthermore, Defendants have presented no evidence that Congress would not have enacted § 353a in the absence of these provisions. Defendants simply point out that the exemption for compounded drugs in § 353a, by its terms, applies only if "the drug meets the requirements of this section." Defendants' Reply at 19.

Defendants infer from this statement that Congress would not have exempted compounded drugs from the FDA's approval process in the absence of the speech-related sections.

The evidence, however, is to the contrary. As Defendants concede, prior to Congress' enactment of the Modernization Act, FDA testing and labeling requirements were not imposed on compounded drugs; the FDA exercised its enforcement discretion to permit pharmacists to compound drugs without meeting these stringent standards. It is difficult for this court to believe that after years of permitting pharmacists to compound drugs without satisfying the FDA's stringent standards, the Government would now enforce these standards in the context of compounding because one of its alleged protections—the restriction of advertising—is unavailable. There is no evidence on the record to support this assumption; indeed, the facts support the opposite conclusion. Therefore, the court finds that the speech-related portions of the § 353a are severable, leaving the remainder of the statute to operate as it was enacted.

CONCLUSION

For the foregoing reasons, the court DENIES Defendants' Motion for Summary Judgment and GRANTS Plaintiffs' Cross-Motion for Summary Judgment, and enjoins the FDA from enforcing the speech-related restrictions contained in §§ 353a(a) and (c).

IT IS SO ORDERED.

APPENDIX C

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEVADA

CV-S-98-01650-JBR (RLH)

WESTERN STATES MEDICAL CENTER PHARMACY, A NEVADA CORPORATION; WOMEN'S INTERNATIONAL PHARMACY, A WISCONSIN CORPORATION; HEALTH PHARMACY, A WISCONSIN CORPORATION; APOTHECURE, A TEXAS CORPORATION; COLLEGE PHARMACY, A COLORADO CORPORATION; LAKESIDE PHARMACY, A TENNESSEE CORPORATION; WEDGEWOOD VILLAGE PHARMACY, A NEW JERSEY CORPORATION, PLAINTIFFS

v.

DONNA E. SHALALA, IN HER OFFICIAL CAPACITY AS SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND MICHAEL A. FRIEDMAN, IN HIS OFFICIAL CAPACITY AS ACTING COMMISSIONER, UNITED STATES FOOD AND DRUG ADMINISTRATION, DEFENDANTS

[Filed: Dec. 18, 1998]

ORDER

On November 19, 1998, Plaintiffs Western States Medical Center Pharmacy, Women's International Pharmacy, Health Pharmacy Apothecure, College Pharmacy, Lakeside Pharmacy, and Wedgewood Village Pharmacy (jointly referred to hereinafter as "Pharmacies") moved (#3) for a temporary restraining

order against Defendants Donna Shalala, Secretary of the United States Department of Health and Human Services and Michael A. Friedman, Acting Commissioner of the United States Food and Drug Administration (jointly referred to hereinafter as the "Government"). The Government opposed (#15) Pharmacies' motion for a temporary restraining order, to which the Pharmacies replied (#17).

In their motion, Pharmacies seek to prevent enforcement of two provisions of the Food and Drug Modernization Act of 1997 (the "Modernization Act," 21 U.S.C. § 353a). The Modernization Act allows a pharmacy to compound drugs, without meeting the approval requirements established for new drugs, under certain conditions. Pharmacies claim that 21 U.S.C. § 353A(c), which allows a pharmacy to compound drugs only if the pharmacy "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug," is an abridgment of speech protected by the First Amendment. In their motion, Pharmacies further claim that 21 U.S.C. § 353a(b)(3) should also not be enforced. Section 353a(b)(3) allows a pharmacy to only distribute "compounded drug products out of the States in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed. . . ." A pharmacy, however, would be allowed to distribute compounded drugs in greater quantity if the State where the drugs is compounded has entered into a memorandum of understanding ("MOU") with the Secretary of Health and Human Services that "addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounding drug

products distributed outside such States. . . ." The Secretary, however, has not yet developed an MOU. Pharmacies argue that the 5 percent limitation should not be enforced until the Secretary actually develops the MOU.

The Government argues the Pharmacies do not have standing to challenge the Modernization Act because the Pharmacies have not demonstrated a realistic danger that the Act will be enforced against them. The Government further argues that the Pharmacies' right to freedom of speech has not been abridged because the First Amendment does not protect advertisements of illegal practices. The Government explains that compounding is illegal unless exempted under the Modernization Act. In order for compounding drugs to be exempt under the Modernization Act, a pharmacy may not advertise the compounding of a particular drug. The Government also argues advertising the compounding of specific drugs. The ingredients used in the Pharmacies' compounded drugs are approved by the Food and Drug Administration (the "FDA"). The specific combinations, proportions, dosages or uses, however, may not have been reviewed by the FDA's approval process.

Section 355(a) of the Federal Food, Drug and Cosmetic Act (the "Food and Drug Act," 21 U.S.C. § 301 et seq.), provides that "No person shall introduce or deliver into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug." Section 321(p) of the Food and Drug Act defines a "new drug" as "any drug . . . not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe and effective for use under the condi-

tions prescribed, recommended, or suggested in the labeling thereof . . . or . . . [a]ny drug . . . which has become so recognized [as safe and effective] but which has not . . . been used to a material extent or for a material time under such conditions." Many of the compounded drugs produced by Pharmacies can properly be classified as new drugs under the Food and Drug Act.

Previously, the Secretary had discretion to make exception to the above requirement, or has not historically enforced these provisions as to compounded drugs. However, in 1997, Congress enacted the Food and Drug Modernization Act of 1997 (the "Modernization Act," 21 U.S.C. § 353a). Section 353a(a) of the Modernization Act provides that a compounded drug need not obtain an approval of an application normally required of a new drug "if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug meets the *requirements of this section* and if the compounding is by . . . a licensed pharmacist in a State licensed pharmacy." (Emphasis added). One of the requirements of this section, 21 U.S.C. § 353a(c) (hereinafter referred to as the "Non-Advertising Provision"), is that the pharmacy may not "advertise or promote the compounding of any particular drug" or promote the compounding service provided by the licensed pharmacist . . ."

STANDING

In *Bland* v. *Fessler*, 88 F.3d 729, 736-37 (9th Cir. 1996), the Ninth Circuit held that a telephone advertiser that used computers to make automated phone calls

had standing under the First Amendment to challenge the constitutionality of a State public utility code prohibiting the use of devices to make automated phone calls even though the State had never enforced the statute against anyone. The Ninth Circuit found that, "one does not have to await the consummation of threatened injury to obtain preventative relief . . . [i]f the injury is certainly impending . . ." *Id.* at 736. The court reasoned when the statute allegedly infringes on freedom of speech, the alleged danger is self-censorship because of fear of prosecution under the statute and is a harm that can be realized without actual prosecution. *Id.* at 737. The court also noted that the telephone advertiser would "face grave consequences for violations of the civil statute, including civil fines and private suits for damages" and that the "State had not suggested that the newly enacted statute would not be enforced." *Id.* at 736 n. 11, 737. The Ninth Circuit concluded that to have standing when challenging the constitutionality of the statute under the First Amendment, plaintiff need only show "an actual well-founded fear that the law will be enforced against them." *Id.* at 737.

In this case, the Government has not indicated that they will not enforce the advertisement ban found in the Modernization Act, and Pharmacies face the same self-censorship due to a fear of prosecution expressed in *Bland*. Additionally, Pharmacies face grave consequences from States for violations of the advertisements ban. States may impose civil fines or revoke Pharmacies' licenses for failure to comply with federal drug safety statutes. Pharmacies have standing under the First Amendment to challenge the Modernization Act's prohibition against advertising compounded

drugs because they face an actual well-founded fear that the Act's Non-Advertising Provision will be enforced against them.

The Government does not allege that advertising a particular compounded drug is inherently misleading. The Government does argue, however, that compounded drugs fall under the definition of "new drug" and cannot be introduced or delivered into interstate commerce without the approval of an application for such drug unless the compounded drug is exempted from the approval process under the Modernization Act. The Government further argues that in order for compounding drugs to be exempt under the Modernization Act, Pharmacies may not advertise the compounding of a particular drug. The Government concludes that because the distribution of compounded drugs by Pharmacies is illegal unless the Modernization exemption applies, the advertisement of a particular compounded drug is not protected by the First Amendment.

The Court agrees that compounded drugs fall under the definition of a "new drug." In *Weinberger* v. *Bentex Pharmaceuticals*, 412 U.S. 645, 652 (1973), the Supreme Court, construing 21 U.S.C. § 321(p), recognized that "whether a particular drug is a 'new drug,' depends in part on the expert knowledge and experience of scientists based on controlled clinical experimentation and backed by substantial support in scientific literature." In *United States* v. *Generix Drug Corporation*, 460 U.S. 453, 461 (1983), the Supreme Court held that all the ingredients of a drug, both active and inactive, are subject to the requirements of § 321(p). While Pharmacies point out that the compounded drugs they distribute are listed in authoritative literature, they also admit

that in many instances the specific drug formulas have been individualized for a specific patient. Pharmacies do not contend that these individualized formulas, or even all the actual formulas listed in the authoritative literature, have undergone the extensive controlled clinical testing necessary so that many of the compounded drugs, with all their ingredients as proportioned, no longer fall within the terms of § 201(p).

The Court also agrees that, prior to the enactment of the Modernization Act, compounding a drug, which could be considered a "new drug," may have been illegal and that the Government used its enforcement discretion to not prosecute such cases when the Government believed that pharmacists were not engaged in manufacturing. By passing the Modernization Act, Congress decided to exempt compounding, under certain conditions, from the normal approval requirements necessary for new drugs. One of those conditions may not be the prohibition of commercial speech unless the Government can assert a substantial reason for the prohibition and also show that the prohibition directly advances that interest. To hold otherwise, would make "commercial speech" unprotectable. The advertisement of any product or service, which is not itself protected by the Constitution, could be banned by the Government with impunity. For example, the Government could make the selling of all products and services illegal except in instances where the selling of the product or service is not advertised, thus eliminating all commercial speech. Once Congress decided to permit compounding, even under limited circumstances such as those found in the Modernization Act, Congress cannot thereafter limit the advertising of compounding without satisfying the remaining *Central Hudson* factors.

Pharmacies, however, also take an untenable position with regards to legality of compounding and its relationship to the prohibition of advertising. Pharmacies argue that since compounding itself is not illegal, prohibiting the advertising of this perfectly legal conduct cannot be justified. Such an argument totally eliminates the last three prongs of the *Central Hudson* test and is contrary to the body of Supreme Court precedent.

While Justice Stevens, who authored the court's opinion in *44 Liquormart* v. *Rhode Island*, 517 U.S. 484 (1996) without a clear majority, "indicated his view that all truthful and not misleading speech was protected by the First Amendment," he dutifully applied all four prongs of the *Central Hudson* test and found that Rhode Island's ban on alcohol price advertisements did not satisfy its third ('directly advances') prong nor its forth ('not more extensive') prong." *E.g.*, *Nordyke* v. *Santa Clara County*, 110 F.3d, 707, 712 (9th Cir. 1997). In concurring, Justice O'Connor, speaking for three other justices, also firmly supported "the *Central Hudson* test in all its four parts." *Id.* The entire *Central Hudson* framework is premised on the notion that advertising of legal activities can be regulated, or even banned, if the government has a substantial interest and the regulation is no more extensive than necessary.

Recently, the Supreme Court upheld an advertising ban even though the underlying activity ws legal. In *Florida Bar* v. *Went For It, Inc.*, 515 U.S. 618 (1995), the Supreme Court upheld a Florida Bar rule that prohibited lawyers from using direct mail to solicit personal injury or wrongful death clients within thirty days of an accident even though the representation of

these clients was not only legal but necessary. The court upheld the ban because it found the Florida Bar's interest in protecting the privacy of potential clients was substantial, and the prohibition no more extensive than necessary. *Id.* at 625-34. If the Government can provide a substantial reason for its ban on adverting specific compounded drugs and show that the prohibition is not more extensive than necessary, the Modernization Act prohibition on advertising could also be upheld.

The Government has asserted a substantial reason for its ban on advertising of specific compounded drugs. The Government asserts that it is protecting the patients from untested and unproven medications. The Government alleges that before a drug is mass marketed, it has a substantial interest to ensure drug safety and effectiveness. The Supreme Court has continuously held that "the Government has a significant interest in protecting the health, safety, and welfare of its citizens. . . ." *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 485 (1995). This Court finds that the Government's asserted interest to protect the public health is substantial.

The Government, however, has not provide any evidence that the regulation on advertising found in the Modernization Act directly advances the governmental interest asserted, or that the regulation is not more extensive than is necessary to serve that interest. In *Liquormart* almost all the Justices agreed that the government bears the burden of showing that the ban on advertising is no more extensive than necessary. *See* 517 U.S. at 507, 516 (Stevens' Opinion); 517 U.S. at 532 (O'Connor concurrence).

As the Supreme Court has explained, in order for a speech restriction to pass muster under the final prong, there must be "a 'fit' between the legislature's ends and the means chosen to accomplish those ends, a fit that is not necessarily perfect, but reasonable; that represents not necessarily the single best disposition but one whose scope is 'in proportion to the interest served,' that employs not necessarily the least restrictive means but a means narrowly tailored to achieve the desired objective." *Florida Bar*, 515 U.S. at 632. In *Florida Bar*, the government fulfilled that obligation by completing a 2-year study of the effects of lawyer advertising on public opinion, conducting hearings, commissioning surveys, reviewing extensive public commentary, and then determining that several changes to its advertising rules were in order. 515 U.S. at 620. This Court does not mean to suggest, however, that the Government's evidence needs to be as extensive. *But see Nordyke*, 110 F.3d at 713 (indicating that to satisfy the fourth prong of *Central Hudson* the government possibly would have to provide a detailed study to substantiate the government's reason for restricting speech). The Court only finds that the Government has offered no evidence that would indicate a reasonable fit between the Government's stated interest and the adverting ban on specific compounded drugs.

Irreparable Harm

The Court must now decide whether Pharmacies have demonstrated the possibility of irreparable harm. In *Elrod* v *Burns*, 427 U.S. 347, 373 (1976), the Supreme Court held that the "loss of First Amendment freedoms, for even minimal periods of time, unquestionably constitutes irreparable injury." *See also S.O.C.*,

Inc. v. *County of Clark*, 152 F.3d 1136, 1148 amended by 160 F.3d 541 (9th Cir. 1998); *Foti* v. *City of Menlo Park*, 146 F.3d 629, 643 (9th Cir. 1998). As the Pharmacies have demonstrated probable success on the merits on their claim that 21 U.S.C. § 353a(c) infringes on their First Amendment right of freedom of speech, they have also demonstrated the possibility of irreparable harm. Plaintiffs have therefore met the conditions necessary to secure a temporary restraining order. Accordingly,

IT IS **ORDERED** that Pharmacies' motion for a temporary restraining order (#3) is PARTIALLY GRANTED in that the Government is temporarily restrained from enforcing 21 U.S.C. § 353a(c).

DATED this 18th day of December 1998.

/s/ JOHNNIE B. RAWLINSON
JOHNNIE B. RAWLINSON
United States District Judge

APPENDIX D

Compliance Policy Guide 7132.16

Manufacture, Distribution, and Promotion of Adultered, Misbranded, or Unapproved New Drugs for Human Use by State-Licensed Pharmacies

BACKGROUND:

This compliance policy guide (CPG) reflects long-standing FDA policy that has been articulated in related CPGs, warning letters, and federal court decisions.

FDA recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner. This traditional activity is not the subject of this CPG. With respect to such activities, it is important to note that 21 U.S.C. 360(g)(1) exempts retail pharmacies from the registration requirements that include, among other things, a mandatory biennial FDA inspection. The exemption applies to "pharmacies" that operate in accordance with state law and dispense drugs "upon prescriptions of practitioners licensed to administer such drugs to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail" (emphasis added). See also 21 U.S.C. Sections 374(a)(2) (exempting pharmacies that meet the foregoing criteria from certain inspection provisions) and

353(b)(2) (exempting drugs dispensed by filling a valid prescription from certain misbranding provisions).

It should be noted, however, that while retail pharmacies that meet the statutory criteria are exempted from certain requirements of the Federal Food, Drug, and Cosmetic Act (Act), they are not the subject of any general exemption from the new drug, adulteration, or misbranding provisions of the Act.

FDA believes that an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing, distributing, and promoting unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that constitute violations of the Act. Some "pharmacies" that have sought to find shelter under and expand the scope of the exemptions identified above, have claimed that their manufacturing, distribution, and marketing practices are only retail dispensing; however, the practices of these entities are far more consistent with those of drug manufacturers and wholesalers than with retail pharmacies. The activities of the self-styled pharmacies are consistent with the activities of manufacturers in that they direct promotional activities at licensed practitioners and patients. The promotional activities include employing detail persons and hiring marketing consultants to promote the company's specialization of compounding specific products or therapeutic classes of drugs. The firms also receive and use in large quantity bulk drug substances to manufacture unapproved drug products and to manufacture drug products in large quantity, in advance of receiving a valid prescription for the products. Moreover, the firms serve physicians and

patients with whom they have no established individual or professional relationship.

When less significant violations of the Act related to a pharmacy have occurred, FDA has worked cooperatively with state regulatory agencies; generally, FDA will continue to defer such actions to state authorities. However, FDA regards the more extreme examples of the foregoing conduct as significant violations that constitute deliberate efforts to circumvent the new drug, adulteration or misbranding provisions of the Act.

There is a very real potential for causing harm to the public health when drug products are manufactured and distributed in commercial amounts without FDA's prior approval and without adequate record keeping (to retrace and recall harmful products), without labeling, or without adequate manufacturing controls to assure the safety, purity, potency, quality, and identity of the drug product. In one recent instance, an outbreak of eye infections in regional hospitals, and the loss of an eye by each of two patients, was attributed to a drug product compounded by a pharmacy.

FDA has issued warning letters to several firms that were clearly manufacturing drugs for human use under the guise of traditional pharmacy practice. For example, one establishment manufactured over 300,000 dosage units of albuterol sulfate and other inhalation therapy drugs per month for 6,000 patients, most of whom live out of state. Another firm manufactured a large quantity of a drug product at dosage levels that have not been determined by adequate and well controlled studies to be effective for the indicated use. A recent inspection of another company operating with a pharmacy license revealed that the firm had hundreds of bulk drug ingredients on hand to manufacture about

165 different products. A review of the manufacturing dates of the "compounded" drugs on hand during the inspection of this firm revealed that 37 products had been produced over a year prior to the inspection, six products had been made between six and eleven months prior to the inspection, and 111 products had no recorded manufacturing date.

The agency has initiated enforcement action when pharmacy practice extends beyond the reasonable and traditional practice of retail pharmacy. The courts have upheld FDA's interpretation in those cases. See *United States* v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979), aff'd. [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) para. 38,207 at 39,117 (11th Cir. 1983); *Cedars N. Towers Pharmacy, Inc.*, v. *United States*, [1978-79 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) para. 38,200 at 38,826 (S.D. Fla. Aug. 28, 1978). *See also United States* v. *Algon Chemical, Inc.*, 879 F.2d 1154 (3d Cir. 1989), *United States* v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988), cert denied. 489 U.S. 1010 (1989), and *United States* v. *Rutherford*, 442 U.S. 544 (1979), regarding limitations on sale of unapproved and otherwise unlawful products to licensed practitioners.

POLICY:

FDA recognizes that a licensed pharmacist may compound drugs extemporaneously after receipt of a valid prescription for an individual patient (i.e., an oral or written order of a practitioner licensed by state law to administer or order the administration of the drug to an individual patient identified and treated by the practitioner in the course of his or her professional practice). Pharmacies that do not otherwise engage in practices that extend beyond the limits set forth in this CPG may

prepare drugs in very limited quantities before receiving a valid prescription, provided they can document a history of receiving valid prescriptions that have been generated solely within an established professional practitioner-patient-pharmacy relationship, and provided further that they maintain the prescription on file for all such products dispensed at the pharmacy as required by state law.

If a pharmacy compounds finished drugs from bulk active ingredient materials considered to be unapproved new drug substances, as defined in 21 CFR 310.3(g), such activity must be covered by an FDA-sanctioned investigational new drug application (IND) that is in effect in accordance with 21 U.S.C. Section 355(i) and 21 CFR 312.

In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, patient-by-patient consultation between physician and pharmacist must result in documentation that substantiates the medical need for the particular variation of the compound.

Pharmacies may not, without losing their status as retail entities, compound, provide, and dispense drugs to third parties for resale to individual patients.

FDA will generally continue to defer to state and local officials regulation of the day-to-day practice of retail pharmacy and related activities. FDA anticipates that cooperative efforts between the states and the agency will result in coordinated investigations, referrals, and follow-up actions by the states.

FDA may, in the exercise of its enforcement discretion, initiate federal enforcement actions against entities and responsible persons when the scope and nature of a pharmacy's activity raises the kinds of concerns normally associated with a manufacturer and that results in significant violations of the new drug, adulteration, or misbranding provisions of the Act. In determining whether to initiate such an action, the agency will consider whether the pharmacy engages in any of the following acts:

1. Soliciting business (e.g., promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products.
2. Compounding, regularly, or in inordinate amounts, drug products that are commercially available in the marketplace and that are essentially generic copies of commercially available, FDA-approved drug products.
3. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA approved facility.
4. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
5. Using commercial scale manufacturing or testing equipment for compounding drug products.
6. Compounding inordinate amounts of drugs in anticipation of receiving prescriptions in relation to the amounts of drugs compounded after receiving valid prescriptions.

7. Offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
8. Distributing inordinate amounts of compounded products out of state.
9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.

The foregoing list of factors is not intended to be exhaustive and other factors may be appropriate for consideration in a particular case.

FDA guidelines and other CPGs interpret or clarify agency positions concerning nuclear pharmacy, hospital pharmacy, shared service operations, mail order pharmacy, and the manipulation of approved drug products.

REGULATORY ACTION GUIDANCE:

Pharmacies engaged in promotion and other activities analogous to manufacturing and distributing drugs for human use are subject to the same provisions of the Act as manufacturers. District offices are encouraged to consult with state regulatory authorities to assure coherent application of this CPG to establishments which are operating outside of the traditional practice of pharmacy.

FDA-initiated regulatory action may include issuing a warning letter, seizure, injunction, and/or prosecution. Charges may include, but need not be limited to, violations of 21 U.S.C. Sections 351(a)(2)(B), 352(a), 352(f)(1), 352(o), and 355(a) of the Act.

Issued: 3/16/92

APPENDIX E

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

File No. DC #98-01650-DAE(RLH)

WESTERN STATES MEDICAL CENTER, A NEVADA CORPORATION; WOMEN'S INTERNATIONAL PHARMACY, A WISCONSIN CORPORATION; HEALTH PHARMACY, A WISCONSIN CORPORATION; APOTHECURE, A TEXAS CORPORATION; COLLEGE PHARMACY, A COLORADO CORPORATION; LAKESIDE PHARMACY, A TENNESSEE CORPORATION; WEDGEWOOD VILLAGE PHARMACY, A NEW JERSEY CORPORATION, PLAINTIFFS-APPELLEES

v.

DONNA E. SHALALA, IN HER OFFICIAL CAPACITY AS SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; JANE E. HENNEY, M.D., IN HER OFFICIAL CAPACITY AS COMMISSIONER, DEFENDANTS-APPELLANTS

Filed: Apr. 27, 2001

Before: SCHROEDER, Chief Judge, HALL, and W. A. FLETCHER, Circuit Judges.

The panel has voted to deny appellants' petition for rehearing en banc. The full court has been advised of the petition for rehearing en banc and no active judge has requested a vote on whether to rehear the matter en banc. Fed. R. App. P. 35.

The petition for rehearing en banc is DENIED.

APPENDIX F

STATUTORY PROVISIONS

1. Section 353a of Title 21, United States Code, provides:

Pharmacy compounding

(a) In general

Sections 351(a)(2)(B), 352(f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding—

(1) is by—

(A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or

(B) a licensed physician,

on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

(2)(A) is by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and

(B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescrip-

tion orders for the compounding of the drug product, which orders have been generated solely within an established relationship between—

(I) the licensed pharmacist or licensed physician; and

(ii)(I) such individual patient for whom the prescription order will be provided; or

(II) the physician or other licensed practitioner who will write such prescription order.

(b) Compounded drug

(1) Licensed pharmacist and licensed physician

A drug product may be compounded under subsection (a) of this section if the licensed pharmacist or licensed physician—

(A) compounds the drug product using bulk drug substances, as defined in regulations of the Secretary published at section 207.3(a)(4) of title 21 of the Code of Federal Regulations—

(i) that—

(I) comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(II) if such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or

(III) if such a monograph does not exist and the drug substance is not a component of a drug

approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (d) of this section;

(ii) that are manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(iii) that are accompanied by valid certificates of analysis for each bulk drug substance;

(B) compounds the drug product using ingredients (other than bulk drug substances) that comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;

(C) does not compound a drug product that appears on a list published by the Secretary in the Federal Register of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective; and

(D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.

(2) Definition

For purposes of paragraph (1)(D), the term "essentially a copy of a commercially available drug product" does not include a drug product in which there is a change, made for an identified individual patient, which

produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.

(3) Drug product

A drug product may be compounded under subsection (a) of this section only if—

(A) such drug product is not a drug product identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product; and

(B) such drug product is compounded in a State—

(i) that has entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or

(ii) that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician.

The Secretary shall, in consultation with the National Association of Boards of Pharmacy, develop a standard

memorandum of understanding for use by the States in complying with subparagraph (B)(i).

(c) Advertising and promotion

A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.

(d) Regulations

(1) In general

The Secretary shall issue regulations to implement this section. Before issuing regulations to implement subsections (b)(1)(A)(i)(III), (b)(1)(C), or (b)(3)(A) of this section, the Secretary shall convene and consult an advisory committee on compounding unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary.

(2) Limiting compounding

The Secretary, in consultation with the United States Pharmacopoeia Convention, Incorporated, shall promulgate regulations identifying drug substances that may be used in compounding under subsection (b)(1)(A)(i)(III) of this section for which a monograph does not exist or which are not components of drug products

approved by the Secretary. The Secretary shall include in the regulation the criteria for such substances, which shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify.

(e) Application

This section shall not apply to—

(1) compounded positron emission tomography drugs as defined in section 321(ii) of this title; or

(2) radiopharmaceuticals.

(f) Definition

As used in this section, the term "compounding" does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling.

2. Section 321(p) of Title 21, United States Code, provides:

(p) The term "new drug" means-

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new

drug" if at any time prior to June 25, 1938, it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

3. Section 331 of Title 21, United States Code, provides, in relevant part:

Prohibited acts

The following acts and the causing thereof are prohibited:

(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.

(b) The adulteration or misbranding of any food, drug, device, or cosmetic in interstate commerce.

(c) The receipt in interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery thereof for pay or otherwise.

(d) The introduction or delivery for introduction into interstate commerce of any article in violation of section 344 or 355 of this title.

* * * * *

4. Section 351 of Title 21, United States Code, provides, in relevant part:

(a) Poisonous, insanitary, etc., ingredients; adequate controls in manufacture

(1) If it consists in whole or in part of any filthy, putrid, of decomposed substance; or (2)(A) if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; or (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopoeia to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess; or (3) if its container is com-

posed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) it bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 379e(a) of this title, or (B) it is a color additive the intended use of which in or on drugs or devices is for purposes of coloring only and is unsafe within the meaning of section 379e(a) of this title; or (5) if it is a new animal drug which is unsafe within the meaning of section 360b of this title; of (6) if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 360b of this title.

(b) Strength, quality, or purity differing from official compendium

If it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standard set forth in such compendium. Such determination as to strength, quality, or purity shall be made in accordance with the tests or methods of assay set forth in such compendium, except that whenever tests or methods of assay have not been prescribed in such compendium, or such tests or methods of assay as are prescribed are, in the judgment of the Secretary, insufficient for the making such determination, the Secretary shall bring such fact to the attention of the appropriate body charged with the revision of such compendium, and if such body fails within a reasonable time to prescribe tests or methods of assay which, in the judgment of the Secretary, are sufficient for purposes of this paragraph, then the Secretary shall promulgate regulations prescribing appropriate tests or methods of assay in accordance

with which such determination as to strength, quality, or purity shall be made. No drug defined in an official compendium shall be deemed to be adulterated under this paragraph because it differs from the standard of strength, quality, or purity therefor set forth in such compendium, if its difference in strength, quality, or purity from such standard is plainly stated on its label. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homeopathic Pharmacopoeia of the United States it shall be subject to the requirements of the United States Pharmacopoeia unless it is labeled and offered for sale as a homeopathic drug, in which case it shall be subject to the provisions of the Homeopathic Pharmacopoeia of the United States and not to those of the United States Pharmacopoeia.

(c) Misrepresentation of strength, etc., where drug is unrecognized in compendium

If it is not subject to the provisions of paragraph (b) of this section and its strength differs from, or its purity or quality falls below, that which it purports or is represented to possess.

(d) Mixture with or substitution of another substance

If it is a drug and any substance has been (1) mixed or packed therewith so as to reduce its quality or strength or (2) substituted wholly or in part therefor.

* * * * *

5. Section 352 of Title 21, United States Code, provides, in relevant part:

Misbranded drugs and devices

A drug or device shall be deemed to be misbranded-

(a) False or misleading label

If its labeling is false or misleading in any particular. Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information directly relates to an indication approved under section 290aa-4 or under section 262(a) of Title 42 for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 290aa-4(a) or in section 262(a) of Title 42 shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term "health care economic information" means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcome of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.

(b) Package form; contents of label

If in package form unless it bears a label containing (1) the name and place of business of the manufacturer, packer, or distributor; and (2) an accurate statement of

the quantity of the contents in terms of weight, measure, or numerical count: *Provided*, That under clause (2) of this paragraph reasonable variations shall be permitted, and exemptions as to small packages shall be established, by regulations prescribed by the Secretary.

(c) Prominence of information on label

If any word, statement, or other information required by or under authority of this chapter to appear on the label or labeling is not prominently placed thereon with such conspicuousness (as compared with other words, statements, designs, or devices, in the labeling) and in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.

* * * * *

(e) Designation of drugs or devices by established names

(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

(ii) the established name and quantity or, if determined to be appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if determined to be appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophen-

detidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if determined to be appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, except that nothing in this subclause shall be deemed to require that any trade secret be divulged, and except that the requirements of this subclause with respect to alphabetical order shall apply only to nonprescription drugs that are not also cosmetics and that this subclause shall not apply to nonprescription drugs not intended for human use.

(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at lease half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of subclause (ii) or (iii) of clause (A) or this

clause is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

* * * * *

(3) As used in subparagraph (1), the term "established name", with respect to a drug or ingredient thereof, means (A) the applicable official name designated pursuant to section 358 of this title, or (B), if there is no such name and such drug, or such ingredient, is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug or of such ingredient, except that where clause (B) of this subparagraph applies to an article recognized in the United States Pharmacopoeia and in the Homeopathic Pharmacopoeia under different official titles, the official title used in the United States Pharmacopoeia shall apply unless it is labeled and offered for sale as homeopathic drug, in which case the official title used in the Homeopathic Pharmacopoeia shall apply.

* * * * *

(f) Directions for use and warnings on label

Unless its labeling bears (1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users, except that where any requirement of clause (1) of this paragraph, as applied

to any drug or device, is not necessary for the protection of the public health, the Secretary shall promulgate regulations exempting such drug or device from such requirement.

(g) Representations as recognized drug; packing and labeling; inconsistent requirements for designation of drug

If it purports to be a drug the name of which is recognized in an official compendium, unless it is packaged and labeled as prescribed therein. The method of packing may be modified with the consent of the Secretary. Whenever a drug is recognized in both the United States Pharmacopoeia and the Homeopathic Pharmacopoeia of the United States, it shall be subject to the requirements of the United States Pharmacopoeia with respect to packaging and labeling unless it is labeled and offered for sale as a homeopathic drug, in which case it shall be subject to the provisions of the Homeopathic Pharmacopoeia of the United States, and not to those of the United States Pharmacopoeia, except that in the event of inconsistency between the requirements of this paragraph and those of paragraph (e) as to name by which the drug or its ingredients shall be designated, the requirements of paragraph (e) shall prevail.

(h) Deteriorative drugs; packing and labeling

If it has been found by the Secretary to be a drug liable to deterioration, unless it is packaged in such form and manner, and its label bears a statement of such precautions, as the Secretary shall by regulations require as necessary for the protection of the public health. No such regulation shall be established for any drug recognized in an official compendium until the

Secretary shall have informed the appropriate body charged with the revision of such compendium of the need for such packaging or labeling requirements and such body shall have failed within a reasonable time to prescribe such requirements.

(i) Drug; misleading container; limitation; offer for sale under another name

(1) If it is a drug and its container is so made, formed, or filled as to be misleading; or (2) if it is an imitation of another drug; or (3) if it is offered for sale under the name of another drug.

(j) Health-endangering when used as prescribed

If is dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.

* * * * *

(n) Prescription drug advertisements: established name; quantitative formula; side effects, contraindications, and effectiveness; prior approval; false advertising; labeling; construction of the Convention on Psychotropic Substances

In the case of any prescription drug distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug a true statement of (1) the established name as defined in paragraph (e) of this section, printed prominently and in type at least half as large as that used for any trade or brand name thereof (2) the formula showing quantitatively each ingredient of such drug to the extent required for labels

under paragraph (e) of this section, and (3) such other information in brief summary relating to side effects contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with the procedure specified in section 371(e) of this title, except that (A) except in extraordinary circumstances, no regulation issued under this subsection shall require prior approval by the Secretary of the content of any advertisement, and (B) no advertisement of a prescription drug, published after the effective date of regulations issued under this subsection applicable to advertisement of prescription drugs, shall with respect to the matters specified in this subsection or covered by such regulations, be subject to the provisions of sections 52 to 57 Title 15. This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 321(m) of this title. Nothing in the Convention on Psychotropic Substances, signed at Vienna, Austria, on February 21, 1971, shall be construed to prevent drug price communications to consumer.

***(o)* Drugs or devices from nonregistered establishments**

If it was manufactured, prepared, propagated, compounded, or processed in an establishment in any State not duly registered under section 360 of this title, if it was not included in a list required by section 360(j) of this title, if a notice or other information respecting it was not provided as required by such section or section 360(k) of this title, or if it does not bear such symbols from the uniform system for identification of devices prescribed under section 360(e) of this title as the Secretary by regulation requires.

(p) Packaging or labeling of drugs in violation of regulations

If it is a drug and its packaging or labeling is in violation of an applicable regulation issued pursuant to section 1472 or 1473 of Title 15.

* * * * *

6. Section 355 of Title 21, United State Code, provides, in relevant part:

New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

* * * * *

7. Section 360 of Title 21, United States Code, provides, in relevant part:

Registration of producers of drugs or devices

(a) Definitions

As used in this section—

(1) the term "manufacture, preparation, propagation, compounding, or processing" shall include repackaging or otherwise changing the container, wrapper, or labeling of any drug package or device package in furtherance of the distribution of the drug or device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user; and

(2) the term "name" shall include in the case of a partnership the name of each partner and, in the case of a corporation, the name of each corporate officer and director, and the State of incorporation.

(b) Annual registration

On or before December 31 of each year every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs, or a device or devices shall register with the Secretary his name, places of business, and all such establishments.

(c) New producers

Every person upon first engaging in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs or a device or devices in any establishment which he owns or operates in any State shall immediately register with the Secretary his name, place of business, and such establishment.

(d) Additional establishments

Every person duly registered in accordance with the foregoing subsections of this section shall immediately register with the Secretary any additional establishment which he owns or operates in any State and in which he begins the manufacture, preparation, propagation, compounding, or processing of a drug or drugs or a device or devices.

(e) Registration number; uniform system for identification of devices intended for human use

The Secretary may assign a registration number to any person or any establishment registered in accordance with this section. The Secretary may also

assign a listing number to each drug or class of drugs listed under subsection (j) of this section. Any number assigned pursuant to the preceding sentence shall be the same as that assigned pursuant to the National Drug Code. The Secretary may by regulation prescribe a uniform system for the identification of devices intended for human use and may require that persons who are required to list such devices pursuant to subsection (j) of this section shall list such devices in accordance with such system.

(f) Availability of registrations for inspection

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this section; except that any list submitted pursuant to paragraph (3) of subsection (j) of this section and the information accompanying any list or notice filed under paragraph (1) or (2) of that subsection shall be exempt from such inspection unless the Secretary finds that such an exemption would be inconsistent with protection of the public health.

(g) Exclusions from application of section

The foregoing subsections of this section shall not apply to—

(1) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in

the regular course of their business of dispensing or selling drugs or devices at retail;

(2) practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in the course of their professional practice;

(3) persons who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in research, teaching, or chemical analysis and not for sale;

(4) any distributor who acts as a wholesale distributor of devices, and who does not manufacture, repackage, process, or relabel a device; or

(5) such other classes of persons as the Secretary may by regulation exempt from the application of this section upon a finding that registration by such classes of persons in accordance with this section is not necessary for the protection of the public health.

In this subsection, the term "wholesale distributor" means any person (other than the manufacturer or the initial importer) who distributes a device from the original place of manufacture to the person who makes the final delivery or sale of the device to the ultimate consumer or user.

(h) Inspection of premises

Every establishment in any State registered with the Secretary pursuant to this section shall be subject to inspection pursuant to section 374 of this title and every such establishment engaged in the manufacture, propagation, compounding, or processing of a drug or drugs or of a device or devices classified in class II or III shall be so inspected by one or more officers or employers duly designated by the Secretary at least once in the two-year period beginning with the date of registration of such establishment pursuant to this section and at least once in every successive two-year period thereafter.

* * * * *

(j) Filing of lists of drugs and devices manufactured, prepared, propagated and compounded by registrants; statements; accompanying disclosures

(1) Every person who registers with the Secretary under subsection (b), (c), or (d) of this section shall, at the time of registration under any such subsection, file with the Secretary a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name (as defined in section 352(e) of this title) and by any proprietary name) which are being manufactured, prepared, propagated, compounded, or processed by him for commercial distribution and which he has not included in any list of drugs or devices filed by him with the Secretary under this paragraph or paragraph (2) before such time of registration. Such list shall be prepared in such form and manner as the Secretary may prescribe and shall be accompanied by—

(A) in the case of a drug contained in the applicable list and subject to section 355 or 360b of this title, or a device intended for human use contained in the applicable list with respect to which a per-

formance standard has been established under section 360d of this title or which is subject to section 360e of this title, a reference to the authority for the marketing of such drug or device and a copy of all labeling for such drug or device;

(B) in the case of any other drug or device contained in an applicable list—

(i) which drug is subject to section 353(b) of this title, or which device is a restricted device, a copy of all labeling for such drug or device, a representative sampling of advertisements for such drug or device, and, upon request made by the Secretary for good cause, a copy of all advertisements for a particular drug product or device, or

(ii) which drug is not subject to section 353(b)(1) of this title or which device is not a restricted device, the label and package insert for such drug or device and a representative sampling of any other labeling for such drug or device;

(C) in the case of any drug contained in an applicable list which is described in subparagraph (B), a quantitative listing of its active ingredient or ingredients, except that with respect to a particular drug product the Secretary may require the submission of a quantitative listing of all ingredients if he finds that such submission is necessary to carry out the purposes of this chapter; and

(D) if the registrant filing a list has determined that a particular drug product or device contained in such list is not subject to section 355 or 360b of

this title, or the particular device contained in such list is not subject to a performance standard established under section 360d of this title or to section 360e of this title or is not a restricted device a brief statement of the basis upon which the registrant made such determination if the Secretary requests such a statement with respect to that particular drug product or device.

(2) Each person who registers with the Secretary under this section shall report to the Secretary once during the month of June of each year and once during the month of December of each year the following information:

(A) A list of each drug or device introduced by the registrant for commercial distribution which has not been included in any list previously filed by him with the Secretary under this subparagraph or paragraph (1) of this subsection. A list under this subparagraph shall list a drug or device by its established name (as defined in section 352(e) of this title) and by any proprietary name it may have and shall be accompanied by the other information required by paragraph (1).

(B) If since the date the registrant last made a report under this paragraph (or if he has not made a report under this paragraph, since February 1, 1973) he has discontinued the manufacture, preparation, propagation, compounding, or processing for commercial distribution of a drug or device included in a list filed by him under subparagraph (A) or paragraph (1); notice of such discontinuance, the date of such discontinuance, and the identity (by established name (as defined in section 352(e) of this

title) any by any proprietary name) of such drug or device.

(C) If since the date of registrant reported pursuant to subparagraph (B) a notice of discontinuance he has resumed the manufacture, preparation, propagation, compounding, or processing for commercial distribution of the drug or device with respect to which such notice of discontinuance was reported; notice of such resumption, the date of such resumption, the identity of such drug or device (each by established name (as defined in section 3529(e) of this title) and by any proprietary name), and the other information required by paragraph (1), unless the registrant has previously reported such resumption to the Secretary pursuant to this subparagraph.

(D) Any material change in any information previously submitted pursuant to this paragraph or paragraph (1).

(3) The Secretary may also require each registrant under this section to submit a list of each drug product which (A) the registrant is manufacturing, preparing, propagating, compounding, or processing for commercial distribution, and (B) contains a particular ingredient. The Secretary may not require the submission of such a list unless he has made a finding that the submission of such a list is necessary to carry out the purposes of this chapter.

* * * * *

8. Section 374 of Title 21, United States Code, provides, in relevant part:

(a) Right of agents to enter; scope of inspection; notice; promptness; exclusions

(1) For purposes of enforcement of this chapter, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, or restricted devices are manufactured, processed, packed, or held, the inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs, nonprescription drugs intended for human use, or restricted devices which are adulterated or misbranded within the meaning of this chapter, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this chapter, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of

this chapter. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this chapter), and research data (other than data relating to new drugs, antibiotic drugs, and devices and subject to reporting and inspection under regulations lawfully issued pursuant to section 355(i) or (k), section 360i, or 360j(g) of this title, and data relating to other drugs or devices which in the case of a new drug would be subject to reporting on inspection under lawful regulations issued pursuant to section 355(j) of this title). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

(2) The provisions of the second sentence of paragraph (1) shall not apply to—

(A) pharmacies which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly the practice engaged in dispensing prescription drugs or devices, upon prescriptions of practitioners licenses to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not, either through a subsidiary or otherwise, manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail;

(B) practitioners licensed by law to prescribe or administer drugs, or prescribe or use devices, as the case may be, and who manufacture, prepare, propagate, compound, or process drugs, or manufacture or process devices, solely for use in the course of their professional practice;

(C) persons who manufacture, prepare, propagate, compound, or process drugs or manufacture or process devices, solely for use in research, teaching, or chemical analysis and not for sale;

(D) such other classes of person as the Secretary may by regulation exempt from the application of this section upon a finding that inspection as applied to such classes of persons in accordance with this section is not necessary for the protection of the public health.

(3) An officer or employee making an inspection under paragraph (1) for purposes of enforcing the requirements of section 350a of this title applicable to infant formulas shall be permitted, at all reasonable times, to have access to and to copy and verify any records—

(A) bearing on whether the infant formula manufactured or held in the facility inspected meets the requirements of section 350a of this title, or

(B) required to be maintained under section 350a of this title.

* * * * *

Supreme Court, U.S.
FILED
SEP 25 2001
CLERK

(2)

No. 01-344

In The

Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN
SERVICES, ET AL.,

Petitioners,

v.

WESTERN STATES MEDICAL CENTER, ET AL.,

Respondents.

On Petition For A Writ Of Certiorari To The United States Court Of Appeals For The Ninth Circuit

BRIEF IN OPPOSITION

MICHAEL A. REITER
Counsel of Record
HOWARD M. HOFFMANN
JASON T. LUNDY
DUANE, MORRIS & HECKSCHER LLP
227 West Monroe Street
Suite 3400
Chicago, Illinois 60606
(312) 499-6700

Attorneys for Respondents

COCKLE LAW BRIEF PRINTING CO., (800) 225-6964
OR CALL COLLECT (402) 342-2831

17 pp

QUESTION PRESENTED FOR REVIEW

Do provisions of the Food and Drug Administration Modernization Act of 1997 that permit compounding only if "the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug" violate the First Amendment?

PARTIES TO THE PROCEEDING AND CORPORATE DISCLOSURE STATEMENT PURSUANT TO RULE 29.6

The Respondents are: Western States Medical Center Pharmacy, a Nevada corporation; Women's International Pharmacy, a Wisconsin corporation; Health Pharmacy, a Wisconsin corporation; College Pharmacy, a Colorado corporation; and Wedgewood Village Pharmacy, a New Jersey corporation.*

None of the Respondents has a parent corporation. None of the Respondents has stockholders that are publicly held companies owning 10% or more of the stock in the corporation.

---

*Counsel for the corporations listed above no longer represent Lakeside Pharmacy and ApotheCure.

TABLE OF CONTENTS

	Page
Question Presented for Review	i
Parties to the Proceeding and Corporate Disclosure Statement Pursuant to Rule 29.6	ii
Table of Contents	iii
Table of Authorities	iv
Statement of the Case	1
Inaccuracies in the Petition	1
Reasons for Denying the Petition	4
Conclusion	10

TABLE OF AUTHORITIES

Page

CASES:

44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484 (1996) 5

Bates v. State Bar of Arizona, 433 U.S. 350 (1977) 7

Bolger v. Youngs Drugs Products Corp., 463 U.S. 60 (1983) 6

Carey v. Population Services Int'l, 431 U.S. 678 (1977) 7

Cedars N. Towers Pharmacy, Inc. v. United States, [1978-79 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978) 4

Central Hudson & Gas Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557 (1980) 4, 5, 6, 8, 10

Children's Legal Found. v. Action for Children's Television, 503 U.S. 913 (1992) 9

City of Cincinnati v. Discovery Network, 507 U.S. 410 (1993) 6

Curran v. Muller, 493 U.S. 1074 (1990) 9

Day v. Holahan, 513 U.S. 1127 (1995) 9

Edenfield v. Fane, 507 U.S. 761 (1993) 6

FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000) 3

Florida Bar v. Went For It, 515 U.S. 618 (1995) 7, 8

Greater New Orleans Broad. Ass'n v. United States, 527 U.S. 173 (1999) 5

Ibanez v. Florida Dep't of Bus. & Prof'l Regulation, 512 U.S. 136 (1994) 6

TABLE OF AUTHORITIES – Continued

Page

In re R.M.J., 455 U.S. 191 (1982) 6

Lorillard Tobacco Co. v. Reilly, 121 S. Ct. 2404 (2001) 5, 7, 8

Nolasco v. United States, 502 U.S. 833 (1991) 9

Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447 (1978) 8

Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999) 3

Rubin v. Coors, 514 U.S. 476 (1995) 6

United States v. Edge Broad. Co., 509 U.S. 418 (1993) 7

United States v. Gainey, 380 U.S. 63 (1965) 9

United States v. Sene X Eleemosynary Corp., 479 F. Supp. 970 (S.D. Fla. 1979) 4

Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748 (1976) 7

Voinovich v. Women's Med. Prof'l Corp., 523 U.S. 1036 (1998) 9

Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998) 3

Washington Legal Found. v. Friedman, 36 F. Supp. 2d 16 (D.D.C. 1999) 3

Washington Legal Found. v. Henney, 56 F. Supp. 2d 81 (D.D.C. 1999), *vacated at* 202 F.3d 331 (D.C. Cir. 2000) 3

Zauderer v. Office of Disciplinary Counsel, 471 U.S. 626 (1985) 6

TABLE OF AUTHORITIES – Continued

Page

STATUTES:

21 U.S.C. §§ 353a(a) and (c) 1, 2, 3

RULES:

S. Ct. R. 10 4

S. Ct. R. 15.2 1

ADMINISTRATIVE AGENCY REGULATIONS:

FDA Compliance Policy Guide § 460.200 2

STATEMENT OF THE CASE

Because Petitioners' Statement of the Case is neither accurate nor complete, Respondents, pursuant to Supreme Court Rule 15.2, correct the inaccuracies in Petitioners' Petition and refer the Court to the facts as set forth in (1) Judge Ezra's order granting Respondents' summary judgment motion (App., 18(a));[1] (2) the Ninth Circuit's opinion (App., 2a-3a); and (3) Respondents' verified complaint.

INACCURACIES IN THE PETITION

1. Contrary to Petitioners' suggestion (Petition, 2, 17-18), this case has *nothing* to do with the distribution of drugs that are not generally recognized as safe and effective. Rather, this case deals *solely* with whether the absolute restrictions on truthful advertising and solicitation contained in the Food and Drug Administration Modernization Act of 1997 ("FDAMA"), 21 U.S.C. §§ 353a(a) and (c), violate the First Amendment.

2.a. Although irrelevant for First Amendment purposes, it is not true, as Petitioners claim, that "[w]hen a pharmacy compounds a drug, the pharmacy creates a 'new drug' because the compounded product is not generally recognized as safe and effective." (Petition, 4.) Nor is it true, as Petitioners suggest (Petition, 4-6), that prior to the enactment of FDAMA, compounding was illegal.

---

[1] Cites to the appendix attached to Petitioners' Petition are designated "App. ___."

b. Compounding was not illegal before FDAMA, even though according to the FDA's Compliance Policy Guide ("CPG") the FDA conferred upon itself discretion to "initiate federal enforcement action against entities and responsible persons when the scope and nature of a pharmacy's activity raise[s] the kinds of concerns normally associated with a manufacturer and that results in significant violation of the new drug adulteration or misbranding provisions of the Act." (App., 76a; FDA Compliance Policy Guide § 460.200, CPG 7132.16.) While Petitioners suggest that before the enactment of FDAMA compounding was illegal, there are no court decisions or statutes that found or made compounding, within the traditional practice of retail pharmacy, illegal. By enacting FDAMA, Congress clarified that compounding within the traditional practice of pharmacy is outside the FDA's jurisdiction. Thus, pursuant to FDAMA, compounded drugs are clearly not new drugs that are subject to FDA approval.

c. Contrary to the claim of Petitioners (Petition, 4-6), before the enactment of Sections 353a(a) and (c), there were no restrictions on the advertising and promotion of compounded drugs by pharmacists or pharmacies. Petitioners' discussion of the CPG at pages 4-6 of their Petition is irrelevant to the First Amendment issues before this Court inasmuch as Petitioners themselves conceded that "Section 353a superseded FDA's policy guide on drug compounding." (Petitioners' Opening Brief in the Ninth Circuit, 12.) The CPG was never law, but simply an unenforceable internal FDA guide for field agents that was not applicable to, or enforceable against, regulatees. Moreover, the courts have not hesitated to declare illegal

the enforcement policies of the FDA based upon its internal guidelines. *See, e.g., FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000) (invalidating on First Amendment grounds FDA's regulations over tobacco); *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999) (invalidating on First Amendment grounds FDA regulation regarding diet supplements); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998) (invalidating on First Amendment grounds policies of FDA and HHS restricting off-label uses of FDA-approved drugs and devices); *Washington Legal Found. v. Friedman*, 36 F. Supp. 2d 16 (D.D.C. 1999); *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81 (D.D.C. 1999) (finding FDA's policies restricting the dissemination of articles and texts relating to off-label use in violation of the First Amendment), *vacated at* 202 F.3d 331 (D.C. Cir. 2000) because FDA conceded on appeal that it had no authority to prosecute manufacturers for violating a normative standard set forth in FDAMA or in the guidelines for continuing medical education.

d. Petitioners claim (Petition, 4-5) that prior to the enactment of FDAMA, the FDA was enforcing the Food, Drug and Cosmetic Act in a way that is consistent with Sections 353a(a) and (c). Petitioners erroneously represent that all that Congress did in enacting those sections was to codify the law that existed prior to the enactment of those sections. Hence, Petitioners argue those sections are not unconstitutional. Petitioners are incorrect. First, there was no constitutional challenge to the way FDA enforced the CPG prior to the enactment of FDAMA, and the assertion that their enforcement was not unconstitutional is without legal support. Second, in support of their

argument, Petitioners rely upon *United States v. Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979) and *Cedars N. Towers Pharmacy, Inc. v. United States*, [1978-79 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978). These cases do not support Petitioners' claim. Neither *Sene X* nor *Cedars* raised any First Amendment issues; and even if they had, both were decided before *Central Hudson & Gas Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980) and the litany of other persuasive commercial speech cases cited at pp. 5-7, *infra*.

3. Contrary to Petitioners' suggestion that "the widespread distribution of drugs that have not first been shown to be safe and effective poses substantial health risks," (Petition, 17), there was *no evidence* whatsoever offered in this case, and no studies of any sort presented or relied upon, to support the claim that the compounding of drugs by licensed pharmacists such as Respondents, in response to a licensed physician's prescription, constitutes a safety hazard. Nor was there any evidence offered or studies adduced to support Petitioners' contention that the total ban on truthful solicitation and advertising "of any particular drug, class of drug or type of drug" will in any way contribute to public health.

REASONS FOR DENYING THE PETITION

Rule 10 of the Supreme Court states that "[A] petition for certiorari will be granted only for compelling reasons." Sup. Ct. R. 10. A petition for a writ of certiorari is rarely granted in a case such as this one "when the error

consists of * * * the misapplication of a properly stated rule of law." *Id.*

This is a classic case of when a petition for certiorari should not be granted. In this case, the parties agree, and two district judges[2] and the unanimous Ninth Circuit held that the controlling rule of law to be applied in this case is the four-part test enunciated in *Central Hudson & Gas Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980). Petitioners, however, claim that two district judges who ruled on this case and the unanimous Ninth Circuit misapplied the rule of law set forth in *Central Hudson*.

This Court has made it abundantly clear in cases that span a twenty-five year history that absolute prohibitions upon truthful commercial speech, such as those that exist in this case, are unconstitutional. *See, e.g., Lorillard Tobacco Co. v. Reilly*, 121 S. Ct. 2404 (2001) (invalidating on First Amendment grounds regulations prohibiting certain outdoor advertising for smokeless tobacco and cigars and regulations involving point-of-sale advertising); *Greater New Orleans Broad. Ass'n v. United States*, 527 U.S. 173 (1999) (invalidating on First Amendment grounds 18 U.S.C. § 1304 and FCC's implementing regulation that prohibited, *inter alia*, radio and television broadcasters from carrying advertising about privately operated commercial casino gaming, regardless of the station's location); 44 *Liquormart, Inc. v. Rhode Island*, 517 U.S. 484

[2] Judge Johnnie B. Rawlinson was a district court judge of Nevada at the time she granted Respondents' motion for a temporary restraining order. Since then she has been a judge on the Ninth Circuit.

(1996) (invalidating on First Amendment grounds two Rhode Island statutes that prohibited the advertising of alcoholic beverage retail prices anywhere other than at point of purchase); *Rubin v. Coors*, 514 U.S. 476 (1995) (invalidating on First Amendment grounds federal statute that prohibited brewers from disclosing on labels the alcoholic content of their beers); *Ibanez v. Florida Dep't of Bus. & Prof'l Regulation*, 512 U.S. 136 (1994) (invalidating on First Amendment grounds Florida regulation that prohibited certain truthful advertising by certified public accountant); *City of Cincinnati v. Discovery Network*, 507 U.S. 410 (1993) (invalidating on First Amendment grounds city ordinance that prohibited the distribution of commercial publications through freestanding news racks located on public property); *Edenfield v. Fane*, 507 U.S. 761 (1993) (invalidating on First Amendment grounds Florida rule that prohibited certified public accountants from engaging in direct, in-person, uninvited solicitation); *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626 (1985) (invalidating on First Amendment grounds Ohio disciplinary rule that prohibited certain truthful advertising but upholding rule to the extent that advertising fails to disclose pertinent facts); *Bolger v. Youngs Drugs Products Corp.*, 463 U.S. 60 (1983) (invalidating on First Amendment grounds 39 U.S.C. § 3001(3)(2) which prohibited the unsolicited mailings to individual's homes concerning contraceptives); *In re R.M.J.*, 455 U.S. 191 (1982) (invalidating on First Amendment grounds rule of Missouri Code of Professional Responsibility that prohibited certain truthful advertising by attorney); *Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557 (1980) (invalidating on First Amendment grounds New York

Public Service Commission order that electric utilities in New York State cease all advertising that promotes the use of electricity); *Carey v. Population Services Int'l*, 431 U.S. 678 (1977) (invaliding on First Amendment grounds a New York statute that prohibited, *inter alia*, the advertisement or display of contraceptives); *Bates v. State Bar of Arizona*, 433 U.S. 350 (1977) (invalidating on First Amendment grounds truthful advertising of routine legal services); *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council*, 425 U.S. 748 (1976) (invalidating on First Amendment grounds Virginia statute that bars advertising prescription drug prices).

The only exceptions to this rule occurred in two circumstances that do not apply in this case. First, this Court has permitted a ban on truthful advertising where the conduct being advertised is illegal. In *United States v. Edge Broad. Co.*, 509 U.S. 418, 421 (1993), this Court held that "federal statutes that prohibit[ed] the broadcast of lottery advertising by a broadcaster licensed to a state that [did] not allow lotteries, while allowing such broadcasting by a broadcaster licensed to a state that sponsors a lottery," did not violate the First Amendment. Because Respondents' compounding is not illegal under any state or federal law, *Edge* is inapplicable.

Second, in three cases this Court has permitted a *limited* restriction on truthful commercial speech. In two of these cases, *Lorillard Tobacco Co. v. Reilly*, 121 S. Ct. 2404 (2001) and *Florida Bar v. Went For It*, 515 U.S. 618 (1995), there were significant studies presented to support the limited prohibitions on commercial speech. No such studies were presented or relied upon in this case. Moreover, in *Lorillard*, this Court, while invalidating on First

Amendment grounds certain prohibitions on outdoor advertising and point-of-sale advertising regulations, upheld a Massachusetts statute that prohibited the sale of tobacco products without direct contact with a salesperson because "Massachusetts [sought] to regulate the placement of tobacco products for reasons *unrelated to the communication of ideas*." 121 S. Ct. at 2429 (emphasis added). Similarly, in *Florida Bar*, a 5-4 decision, this Court upheld a Florida Bar Rule that prohibited personal injury lawyers from sending targeted direct-mail solicitations to victims and their relatives *for 30 days* following an accident or disaster. 515 U.S. at 635.

By contrast, the unprecedented, unlimited speech and advertising restrictions upon truthful speech found to be unconstitutional by two federal judges and the unanimous Ninth Circuit in this case were not supported by *any* studies, depositions, affidavits or any testimony in the record. Moreover, those restrictions relate solely to the communication of ideas, and they are not, as in *Lorillard*, focused on the protection of minors from demonstrably harmful conduct.

Finally, in *Ohralik v. Ohio State Bar Ass'n*, 436 U.S. 447, 449 (1978), a case decided before *Central Hudson*, this Court upheld application of Ohio disciplinary rules to lawyers who in-person solicited potential personal injury clients "at the hospital room or the accident site, or any other situation that breeds undue influence by attorneys or their agents or runners." Nothing in the present case has anything to do with situations that breed "undue influence."

Petitioners state that because "the court of appeals has held an Act of Congress unconstitutional [t]hat action alone warrants this Court's review." (Petition, 25.) Petitioners cite *United States v. Gainey*, 380 U.S. 63 (1965) for that proposition. That is not a fair reading of that case. In *Gainey*, this Court upheld, on Fifth Amendment grounds, two federal statutes that permitted conviction for certain illegal activities based upon a person's unexplained presence at an illegal still. Unlike this case, there was not a clear line of precedent for the Court to rely on. In that context, this Court said that it "granted certiorari * * * to review the exercise of the grave power of annulling an Act of Congress." 380 U.S. at 65. The Court did not say that whenever an Act of Congress is held unconstitutional "that alone warrants the Court's review." If that had been intended, then Supreme Court Rule 10 would have so provided. In fact, this Court has denied petitions for a writ of certiorari where both federal and state statutes have been declared unconstitutional by the lower courts. *See, e.g., Voinovich v. Women's Med. Prof'l Corp.*, 523 U.S. 1036 (1998) (state statute); *Day v. Holahan*, 513 U.S. 1127 (1995) (state statute); *Children's Legal Found. v. Action for Children's Television*, 503 U.S. 913 (1992) (FCC order); *Curran v. Muller*, 493 U.S. 1074 (1990) (state statute); *Nolasco v. United States*, 502 U.S. 833 (1991) (federal statute, 18 U.S.C. § 3013, held unconstitutional by Ninth Circuit).

In this case, Petitioners have had their positions heard and reviewed separately by two federal judges, and three judges of the Ninth Circuit, one of whom is the Chief Judge. Each judge followed this Court's decisions and rejected Petitioners' arguments. Petitioners also filed

a motion for reconsideration in the Ninth Circuit and that, too, was denied. Petitioners do nothing more than disagree with how the courts below applied *Central Hudson*. This is a classic claim of "the misapplication of law" which merits the denial of certiorari.

This Court does not sit as yet another circuit court of appeals to review the decisions of the lower courts because the Petitioners disagree with the outcome. This case raises not one new principle of law. Every time lower courts unanimously find legislation to violate this Court's clear admonition in *Central Hudson*, it is not an invitation to request this Court once again to review the decisions of the lower courts. We respectfully suggest that governmental bodies must follow the law that this Court has settled in twenty-five years of precedent. No clearer message can be sent than by a simple denial of certiorari in this case.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted,

MICHAEL A. REITER
Counsel of Record
HOWARD M. HOFFMANN
JASON T. LUNDY
DUANE, MORRIS & HECKSCHER LLP
227 West Monroe Street
Suite 3400
Chicago, Illinois 60606
(312) 499-6700

Attorneys for Respondents

Supreme Court, U.S.
FILED
OCT 9 2001

(3)

No. 01-344

In the Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

REPLY BRIEF FOR THE PETITIONERS

THEODORE B. OLSON
Solicitor General
Counsel of Record
Department of Justice
Washington, D.C. 20530-0001
(202) 514-2217

TABLE OF AUTHORITIES

Cases:	Page
Central Hudson Gas & Elec. Corp. v. *Public Serv. Comm'n*, 447 U.S. 557 (1980)	6
Children's Legal Found., Inc. v. *Action for Children's Television*, 503 U.S. 913 (1992)	2
Florida Bar v. *Went For It, Inc.*, 515 U.S. 618 (1995)	7
44 Liquormart, Inc. v. *Rhode Island*, 517 U.S. 484 (1996)	6
Greater New Orleans Broad. Ass'n v. *United States*, 527 U.S. 173 (1999)	6
Lorillard Tobacco Co. v. *Reilly*, 121 S. Ct. 2404 (2001)	6, 7, 8
Nolasco v. *United States*, 502 U.S. 833 (1991)	2
Ohralik v. *Ohio State Bar Ass'n*, 436 U.S. 447 (1978)	7
Professionals & Patients for Customized Care v. *Shalala*, 56 F.3d 592 (5th Cir. 1995)	4, 5
Rubin v. *Coors*, 514 U.S. 476 (1995)	6
United States v. *Algon Chem., Inc.*, 879 F.2d 1154 (3d Cir. 1989)	4
United States v. *Edge Broad. Co.*, 509 U.S. 418 (1993)	6, 7
United States v. *Gainey*, 380 U.S. 63 (1965)	2
United States v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1998)	4
United States v. *Rutherford*, 442 U.S. 544 (1979)	2, 8
United States v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983)	4
Weinberger v. *Bentex Pharm.*, 412 U.S. 645 (1973)	4

Case—Continued:	Page
Weinberger v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973)	2, 4, 8
Constitution, statutes and rule:	
U.S. Const. Amend. I	1-2
Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.*	1
21 U.S.C. 321(p)	4
21 U.S.C. 331(d)	4
21 U.S.C. 355(a)	4
Food and Drug Administration Modernization Act of 1997, 21 U.S.C. 353a *et seq.*:	
21 U.S.C. 353a (Supp. V 1999)	1, 3, 4, 5, 6, 7
21 U.S.C. 353a(a) (Supp. V 1999)	1, 6
21 U.S.C. 353a(c) (Supp. V 1999)	1, 7
Sup. Ct. R. 10	5
Miscellaneous:	
143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997)	5
Robert L. Stern et al., *Supreme Court Practice* (7th ed. 1993)	3

In the Supreme Court of the United States

No. 01-344

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

REPLY BRIEF FOR THE PETITIONERS

The Food and Drug Administration Modernization Act of 1997 (FDAMA), 21 U.S.C. 353a (Supp. V 1999), provides a limited exemption from the new drug approval (and certain other) requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, for drugs compounded by pharmacists. This case concerns the constitutionality of FDAMA's limitation of that exemption to pharmacists who do not solicit prescriptions for or advertise particular compounded drugs. 21 U.S.C. 353a(a) and (c) (Supp. V 1999).

The court of appeals erroneously held that the solicitation and advertising limitations on the new statutory exemption are unconstitutional under the First Amend-

ment. See Pet. 16-25. In striking down those limitations, the court of appeals upset the careful balance that Congress established in specifying the point at which potentially harmful drug products should be subject to the FDCA's generally applicable new drug approval requirements. See Pet. 11-16. Those requirements are the linchpin of the Nation's laws regulating the manufacturing and distribution of drugs and thus a central component of Congress's efforts in the FDCA to protect the public health and safety. See generally *United States* v. *Rutherford*, 442 U.S. 544 (1979); *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973). The court of appeals' mistaken "exercise of the grave power of annulling an Act of Congress" warrants this Court's review, particularly because it arises in the critical context of protecting public health and safety. *United States* v. *Gainey*, 380 U.S. 63, 65 (1965).

1. Respondents take issue (Br. in Opp. 9) with the contention (Pet. 11, 25) that the decision of the court of appeals warrants review because that court held an Act of Congress unconstitutional. They point to two instances in which (they assert) this Court has denied petitions seeking review of the invalidation of federal statutes. See Br. in Opp. 9 (citing *Children's Legal Found., Inc.* v. *Action for Children's Television (ACT)*, 503 U.S. 913 (1992), and *Nolasco* v. *United States*, 502 U.S. 833 (1991)). In one of those cases, however, the petitioner did not seek review of the appellate court's invalidation of a federal statute; the petitioner sought review only of the court's holding that the trial court was not required to define reasonable doubt. See Pet. at i-ii, *Nolasco* v. *United States*, *supra* (No. 90-8104). In the other case, the respondents opposed certiorari on the ground that the matter had been remanded to the Federal Communications Commission and the court of

appeals' decision was therefore interlocutory, see Br. of Resp. ACT, et al. at 18, *Children's Legal Found., Inc.* v. *ACT*, *supra* (No. 91-833), which is not true of the decision in this case. Thus, neither of the cases cited by respondents provides any basis for this Court to depart from its virtually uniform practice of granting the government's request for review of an appellate decision that holds an Act of Congress unconstitutional. See Robert L. Stern et al., *Supreme Court Practice* 185 (7th ed. 1993).

Moreover, as noted in the petition, this Court's review is particularly warranted here, because the Act of Congress that the court of appeals invalidated is designed to protect the public health and safety from potentially dangerous drugs and to provide adequate and appropriate incentives for those who manufacture and promote new drugs to bear the costs of demonstrating the safety and efficacy of those drugs. See Pet. 12, 15, 19-20, 25. Section 353a embodies a carefully balanced congressional effort to preserve the effectiveness and integrity of the FDCA's new drug approval process, and, at the same time, to ensure the availability of compounded drugs for those individual patients who, for particularized medical reasons, cannot use commercially available products that have already been approved by the FDA. See Pet. 11-16. The new drug approval requirements are at the core of the Nation's laws regulating the manufacturing and distribution of drugs. By unduly limiting Congress's authority to define the scope of those provisions, the decision of the court of appeals impermissibly interferes with important congressional efforts to protect and to promote public health and safety.

2. Respondents attempt to minimize the importance of the court of appeals' decision by disputing (Br. in

Opp. 1) that compounded drugs are "new drugs" subject to the FDCA's pre-market approval requirements. Respondents also take issue (*id.* at 1-2) with the related conclusion that, before enactment of Section 353a, it was illegal to distribute compounded drugs in interstate commerce without complying with those requirements.

In fact, compounded drugs *are* "new drugs" because they are "not generally recognized * * * as safe and effective for use under the conditions prescribed." 21 U.S.C. 321(p). A drug's safety and effectiveness must be demonstrated by controlled clinical trials conducted by qualified experts. See *Hynson, Westcott & Dunning*, 412 U.S. at 630; *Weinberger* v. *Bentex Pharm.*, 412 U.S. 645, 652 (1973). Neither the clinical impressions of practicing physicians nor the fact that a number of physicians throughout the country prescribe a product establishes that it is generally recognized as safe and effective. See *Hynson, Westcott & Dunning*, 412 U.S. at 630; *United States* v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970, 977 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12 1983).

Therefore, before enactment of Section 353a, several courts of appeals had determined that compounded drugs are "new drugs," which are subject to the FDCA's pre-market approval requirements. See *Professionals & Patients for Customized Care* v. *Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995); *United States* v. *Algon Chem. Inc.*, 879 F.2d 1154, 1158 (3d Cir. 1989); *United States* v. *9/1 Kg. Containers*, 854 F.2d 173, 179 (7th Cir. 1998); 21 U.S.C. 355(a). Distribution of compounded drugs in interstate commerce without the approval of the FDA was thus illegal before enactment of Section 353a. See 21 U.S.C. 331(d), 355(a). Section 353a

establishes an exemption from FDA approval for compounded drugs but subjects that exemption to reasonable conditions, including that particular compounded drugs not be advertised and promoted in the manner that characterizes the manufacture and distribution of new drugs.*

3. Respondents also contend (Br. in Opp. 4-5) that certiorari is not warranted because, in their view, the government seeks review of only "the misapplication of a properly stated rule of law." Sup. Ct. R. 10. That mischaracterizes the government's position. Review is sought to correct a mistaken exercise of the greatest power possessed by the federal courts—the power to

---

* As discussed in the petition (at 14-15, 18-19), Section 353a "bring[s] the legal status of compounding in line with FDA's longstanding enforcement policy," 143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997) (Sen. Kennedy), pursuant to which the FDA did not enforce the FDCA's new drug approval requirements against pharmacies engaged in traditional compounding on an individualized basis in response to the medical needs of particular patients. See Pet. App. 71a; *Professionals & Patients*, 56 F.3d at 593 n.3. The FDA did take action, however, when compounding was outside the scope of normal pharmacy practice and compounded drugs were mass-produced and distributed in a manner tantamount to the manufacture of unapproved new drugs. Pet. App. 73a-74a. Among the factors that the FDA considered in determining whether a pharmacy was manufacturing drugs rather than engaging in traditional compounding was whether the pharmacy was "[s]oliciting business (e.g. promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products." *Id.* at 76a. Thus, contrary to respondents' contention (Br. in Opp. 2), there were "restrictions on the advertising and promotion of compounded drugs by pharmacists" before enactment of Section 353a. As respondents acknowledge, "there was no constitutional challenge" to those restrictions (*id.* at 3), and there are no judicial decisions that call into question their constitutionality.

declare an Act of Congress unconstitutional—in the critical context of important laws promoting the public health and safety.

Respondents are also incorrect in suggesting (Br. in Opp. 5) that an erroneous application of the test for determining the constitutionality of restrictions on commercial speech set out in *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557 (1980), is the kind of "misapplication of a properly stated rule of law" for which certiorari is rarely granted. On the contrary, this Court has repeatedly granted certiorari to review application of the general *Central Hudson* test to particular statutory contexts, especially where the constitutionality of an Act of Congress is at issue. See, *e.g.*, *Lorillard Tobacco Co.* v. *Reilly*, 121 S. Ct. 2404 (2001); *Greater New Orleans Broad. Ass'n* v. *United States*, 527 U.S. 173 (1999); *44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484 (1996); *Rubin* v. *Coors*, 514 U.S. 476 (1995); *United States* v. *Edge Broad. Co.*, 509 U.S. 418 (1993).

Respondents mistakenly rely on what they assert is settled law that "absolute prohibitions upon truthful commercial speech, such as those that exist in this case, are unconstitutional." Br. in Opp. 5. As an initial matter, Section 353a does not impose an absolute prohibition upon speech. Rather, it provides a limited exemption for pharmaceutical compounding from the FDCA's otherwise generally applicable provisions governing the distribution of "new drugs" in interstate commerce, good manufacturing practices, and adequate directions for use. See 21 U.S.C. 353a(a) (Supp. V 1999). That exemption is subject to certain conditions, which include that the prescription for the compounded product must be "unsolicited," 21 U.S.C. 353a(a) (Supp. V 1999), and that the compounder may "not advertise or promote the compounding of any particular drug, class of drug, or type of drug" (21 U.S.C. 353a(c) (Supp. V 1999)). Pharmacies remain free, however, to solicit prescriptions for and to advertise particular compounded products provided that they (like others who manufacture new drugs and introduce them into interstate commerce) comply with the FDCA's new drug approval and related requirements.

Furthermore, this Court has never held that prohibitions upon truthful commercial speech are per se unconstitutional, or even that they are subject to strict scrutiny. Rather, the Court has analyzed such prohibitions under the four-part *Central Hudson* test. See *Lorillard*, 121 S. Ct. at 2421 (rejecting petitioners' request that the Court apply strict scrutiny rather than *Central Hudson*). Although the Court has found restrictions on commercial speech to be unconstitutional in some cases, it has not invariably reached that conclusion, as even respondents acknowledge. See Br. in Opp. 7-8 (citing *Lorillard*, 121 S. Ct. at 2429; *Florida Bar* v. *Went For It, Inc.*, 515 U.S. 618 (1995); *United States* v. *Edge Broad. Co.*, 509 U.S. 418 (1993); *Ohralik* v. *Ohio State Bar Ass'n*, 436 U.S. 447 (1978)).

4. In order to determine whether a limitation on commercial speech is permissible under the First Amendment, a court must carefully apply the general principles set forth in *Central Hudson* and this Court's other commercial speech cases to the particular limitation that is challenged. As explained in the petition, the court of appeals misapplied those principles in striking down Section 353a.

In particular, the court of appeals erroneously failed to credit as substantial the government's interest in preserving the integrity of the drug approval process by preventing the widespread distribution of drugs that

have not been proven safe and effective, on the one hand, and permitting the compounding of drugs in limited circumstances to address the particularized medical needs of individual patients, on the other. See Pet. 16-19. The court of appeals concluded (and respondents continue to contend (Br. in Opp. 4, 7, 8)) that the government presented insufficient evidence to demonstrate that the widespread distribution of drugs that have not been proven safe and effective poses substantial health risks. But that is a fundamental premise of the FDCA, the validity of which this Court itself has acknowledged. See *Rutherford*, 442 U.S. at 556-557; *Hynson, Westcott & Dunning*, 412 U.S. at 619, 622. The court of appeals had no basis to insist that the government introduce evidence in court to establish the manifest importance of that central purpose of the FDCA. See Pet. 17-18; see also *Lorillard*, 121 S. Ct. at 2422 (explaining that restrictions on commercial speech may be justified "based solely on history, consensus, and 'simple common sense'").

Because of its failure to credit the government's substantial interest in preserving both the integrity of the drug approval process and the availability of compounding on an individualized basis in response to particular medical needs, the court of appeals also erroneously concluded that limiting the compounding exemption to pharmacies that do not promote particular compounded products does not directly and materially advance the government's interests and is not narrowly tailored. See Pet. 19-25. In fact, Congress properly concluded that advertising and promotion of a particular compounded drug to the public reasonably identifies the point at which the interest in preserving the integrity of the drug approval requirements outweighs the interest in protecting the availability of

traditional pharmaceutical compounding in response to the special medical needs of identified individuals. That determination reflects the judgment by Congress that advertising and promotion of particular drugs are characteristics of manufacturing, as distinguished from traditional pharmacy compounding in response to particularized medical needs. See Pet 14-15. It also reflects the FDA's prior enforcement experience (see Pet. 4-5), and conforms to the FDCA's premise that those who promote and seek to profit from an expanded market for new drugs should be required and encouraged to bear the cost of proving that those drugs are safe and effective before they are widely disseminated in interstate commerce. See Pet. 12, 15-16. The court of appeals incorrectly rejected those reasonable congressional determinations and improperly invalidated as unconstitutional an Act of Congress designed to promote the public health and safety. That decision warrants this Court's review.

* * * * *

For the reasons stated above and in the petition for a writ of certiorari, the petition should be granted.

Respectfully submitted.

THEODORE B. OLSON
Solicitor General

OCTOBER 2001

Supreme Court, U.S.
FILED
DEC 13 2001
CLERK

(4)

No. 01-344

IN THE SUPREME COURT OF THE UNITED STATES

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

BRIEF FOR THE PETITIONERS

RECEIVED
SUPREME COURT, U.S.
POLICE DEPARTMENT
DEC 13 2001
A.M. 7 8 9 10 11 12 1 2 3 4 5 6 P.M.
1915

THEODORE B. OLSON
Solicitor General
Counsel of Record

ROBERT D. McCALLUM, JR.
Assistant Attorney General

EDWIN S. KNEEDLER
Deputy Solicitor General

MATTHEW D. ROBERTS
Assistant to the Solicitor General

DOUGLAS N. LETTER
KATHERINE S. DAWSON
Attorneys

Department of Justice
Washington, D.C. 20530-0001
(202) 514-2217

ALEX M. AZAR II
General Counsel
U.S. Department of Health
and Human Services

DANIEL E. TROY
Chief Counsel

PATRICIA J. KAEDING
Associate Chief Counsel
U.S. Food & Drug
Administration
Rockville, MD 20857

56pp

QUESTION PRESENTED

The Food and Drug Administration Modernization Act of 1997 (FDAMA), 21 U.S.C. 353a (Supp. V 1999), provides a limited exemption from the new drug approval (and certain other) requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 et seq., for drugs compounded by pharmacists. The question presented is whether FDAMA's limitation of that exemption to pharmacists who do not solicit prescriptions for or advertise particular compounded drugs, 21 U.S.C. 353a(a) and (c) (Supp. V 1999), is consistent with the First Amendment.

PARTIES TO THE PROCEEDINGS

Petitioners are Tommy G. Thompson, Secretary of Health and Human Services, and Bernard A. Schwetz, Acting Principal Deputy Commissioner, United States Food and Drug Administration. Respondents are Western States Medical Center, Women's International Pharmacy, Health Pharmacy, Apothecure, College Pharmacy, Lakeside Pharmacy, and Wedgewood Village Pharmacy.

IN THE SUPREME COURT OF THE UNITED STATES

No. 01-344

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

BRIEF FOR THE PETITIONERS

OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-15a) is reported at 238 F.3d 1090. The opinion of the district court (Pet. App. 16a-59a) is reported at 69 F. Supp. 2d 1288. The opinion of the district court granting respondents' motion for a temporary restraining order (Pet. App. 60a-70a) is unreported.

JURISDICTION

The judgment of the court of appeals was entered on February 6, 2001. A petition for rehearing was denied on April 27, 2001 (Pet. App. 78a-79a). On July 15, 2001, Justice O'Connor extended the time within which to file a petition for a writ of certiorari to and including August 25, 2001. The petition was filed on August

24, 2001, and was granted on October 29, 2001. The jurisdiction of this Court rests on 28 U.S.C. 1254(1).

CONSTITUTIONAL AND STATUTORY PROVISIONS INVOLVED

The First Amendment to the United States Constitution provides that "Congress shall make no law * * * abridging the freedom of speech." The pertinent provisions of the Food and Drug Administration Modernization Act of 1997, 21 U.S.C. 353a (Supp. V 1999), and the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 et seq., are reprinted in the appendix to the petition for a writ of certiorari. Pet. App. 80a-107a.

STATEMENT

1. a. The Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 et seq., establishes a comprehensive scheme for the regulation of drug manufacturing, labeling, marketing, and distribution in order to protect the public health and safety. The FDCA defines a "new drug" as "[a]ny drug * * * not generally recognized * * * as safe and effective for use under the conditions prescribed." 21 U.S.C. 321(p)(1). The FDCA generally requires that, before a new drug may be introduced into interstate commerce, the manufacturer or distributor must obtain the approval of the Secretary of Health and Human Services, acting through the Food and Drug Administration (FDA). See 21 U.S.C. 355(a), 331(d). To obtain that approval, the manufacturer or distributor must demonstrate to the FDA's satisfaction that the drug is both safe and effective for each intended use. See 21 U.S.C. 355(b) (1994 & Supp. V 1999); Weinberger v. Hynson, Westcott & Dunning, Inc., 412

U.S. 609, 613 (1973). The prohibition on introducing new drugs that have not been approved by the FDA applies to all new drugs except those for which Congress has created an exemption. See United States v. Rutherford, 442 U.S. 544, 551 (1979).

The FDCA also imposes standards for the manufacturing and labeling of drugs to ensure that manufacturing processes and drug ingredients are safe and effective and that physicians and consumers have adequate information about drug contents, uses, and effects. See 21 U.S.C. 351, 352 (1994 & Supp. V 1999). The FDCA prohibits the sale and distribution of "adulterated" or "misbranded" drugs. See 21 U.S.C. 331 (1994 & Supp. V 1999).

In addition, to facilitate regulatory oversight, the FDCA imposes registration, inspection, and reporting requirements on drug manufacturers. See 21 U.S.C. 360 (1994 & Supp. V 1999) (requiring drug manufacturers to register with the Secretary); 21 U.S.C. 360(h) (subjecting drug manufacturers to at least one government inspection every two years); 21 U.S.C. 360(j) (1994 & Supp. V 1999) (requiring each registered drug manufacturer to "file with the Secretary a list of all drugs" that it manufactures for commercial distribution).

The FDCA contains a limited exemption from its registration and some of its inspection requirements for pharmacies that comply with state regulations and dispense drugs "upon prescriptions of practitioners licensed to administer such drugs" and that do not "manufacture" or "compound" drugs other than in "the regular course of their business of dispensing or selling drugs * * * at retail."

21 U.S.C. 360(g)(1), 374(a)(2)(A). There is no general exemption for pharmacies, however, from the FDCA's new drug approval, misbranding, and adulteration provisions. 21 U.S.C. 351, 352, 355 (1994 & Supp. V 1999); Pet. App. 72a (1992 FDA Compliance Policy Guide).

b. Compounding is a process by which a pharmacist "combines, mixes, or alters ingredients to create a certain medication for a patient." Professionals & Patients for Customized Care v. Shalala, 847 F. Supp. 1359, 1361 (S.D. Tex. 1994), aff'd, 56 F.3d 592 (5th Cir. 1995). The process encompasses a range of pharmacy activities, including the modification of approved drugs "to provide medications that are not commercially available, such as diluted dosages for children, or to alter the form of a medication for easier consumption." Ibid.

When a pharmacy compounds a drug, the pharmacy creates a "new drug" because the compounded product is not "generally recognized, among experts * * *, as safe and effective." See 21 U.S.C. 321(p)(1). A drug that differs in any material way (including in composition, effect, or intended use) from an approved drug is a new drug that must independently be established to be safe and effective. See United States v. Generix Drug Corp., 460 U.S. 453, 460-461 (1983) (determination whether a product is a new drug takes into account both active and inactive ingredients); 21 C.F.R. 310.3(h) (discussing factors that make a drug a "new drug"). Even a drug that is identical to an approved product is a new drug that must be independently established as safe and effective if it is

produced by a different manufacturer. See USV Pharm. Corp. v. Weinberger, 412 U.S. 655, 664 (1973) ("[Section 355] when applied to [a new drug application] is personal to the manufacturer who files it. Section [355], in other words, addresses itself to drugs as individual products."); Pharmanex v. Shalala, 221 F.3d 1151, 1157 (10th Cir. 2000) (the new drug approval process is manufacturer-specific). A newly created, customized compounded drug will not have been subjected to the controlled clinical trials that are necessary to establish its safety and effectiveness. See Hynson, Westcott & Dunning, 412 U.S. at 630; Weinberger v. Bentex Pharm., Inc., 412 U.S. 645, 652 (1973). Although the prescribing physician presumably believes the compounded product is appropriate for the patient receiving the prescription, neither the impressions of practicing physicians nor the fact that a number of physicians throughout the country prescribe a compounded product is sufficient to establish that it is generally recognized as safe and effective. See Hynson, Westcott & Dunning, 412 U.S. at 630; United States v. Sene X Eleemosynary Corp., 479 F. Supp. 970, 977 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983).

For those reasons, prior to the enactment of the Food and Drug Administration Modernization Act of 1997 (FDAMA), Pub. L. No. 105-115, 111 Stat. 2296, several courts of appeals had confirmed that compounded drugs are "new drugs" subject to the FDCA's premarket approval requirements. See Professionals & Patients for Customized Care v. Shalala, 56 F.3d 592, 593 n.3 (5th Cir. 1995); United

States v. Algon Chem. Inc., 879 F.2d 1154, 1158 (3d Cir. 1989); United States v. 9/1 Kg. Containers, 854 F.2d 173, 179 (7th Cir. 1988); see also United States v. Baxter Healthcare Corp., 901 F.2d 1401, 1410-1411 (7th Cir. 1990) (reconstitution and freezing of already approved drug creates new drug). Introduction of compounded drugs into interstate commerce without the approval of the FDA was thus illegal before enactment of FDAMA, see Professionals & Patients, 56 F.3d at 593 n.3; Pet. App. 72a, and it remains illegal today unless the requirements in Section 353a are satisfied.

The FDA nevertheless recognized that compounding can serve an important public purpose for which the health benefits outweigh the risks if the compounding is performed in response to a valid prescription in order to meet the medical needs of an individual patient for whom commercially available drugs are inadequate. See Pet. App. 71a. Therefore, "the FDA as a matter of policy [did] not historically [bring] enforcement actions against pharmacies engaged in traditional compounding." 56 F.3d at 593 n.3.

The FDA did take action, however, when compounding was outside the scope of normal pharmacy practice and compounded drugs were mass-produced and distributed in a manner tantamount to the manufacture of unapproved new drugs. See Pet. App. 73a-74a. The FDA issued warning letters, see id. at 73a, and sometimes brought judicial enforcement actions against pharmacies that engaged in drug manufacturing under the guise of compounding. E.g., Sene X, 479 F. Supp. at 978; Cedars North Towers Pharmacy, Inc. v. United

States, [1978-79 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,828 (S.D. Fla. Aug. 28, 1978).

Among the factors that the FDA considered in determining whether a pharmacy was engaged in conduct tantamount to manufacturing drugs rather than in traditional compounding were whether the pharmacy was "[s]oliciting business (e.g., promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products." Pet. App. 76a. Other considerations included the extent to which the pharmacy was compounding drug products that were essentially copies of a commercially available drug product, was compounding drugs in advance of receiving valid prescriptions, or was distributing compounded products out of State. Id. at 76a-77a.

2. Congress addressed the compounding issue when it enacted FDAMA in 1997. The section of FDAMA at issue in this case, now codified at 21 U.S.C. 353a (Supp. V 1999), was intended to "bring the legal status of compounding in line with FDA's longstanding enforcement policy of regulating only drug manufacturing, not ordinary pharmacy compounding." 143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997) (statement of Sen. Kennedy). Section 353a seeks to "ensure continued availability of compounded drug products as a component of individualized therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. 94 (1997); accord S. Rep. No. 43, 105th Cong., 1st Sess. 67 (1997).

Rather than leaving to the enforcement discretion of the FDA the determination of when compounding should be permitted, Congress chose to delineate in the FDCA itself the limited circumstances under which pharmacy compounding would be exempt as a matter of law from certain requirements that apply to drug manufacturers. Thus, if specified conditions are met, Section 353a exempts compounded drug products from the FDCA's provisions governing new drug approval, good manufacturing practice, and adequate directions for use. Under those conditions, which echo the FDA's pre-1997 approach to compounding, (1) the compounding must be performed by a licensed pharmacist or physician based on a valid prescription made by a licensed practitioner, see 21 U.S.C. 353a(a)(1) (Supp. V 1999); (2) the compounding must use only ingredients that comply with various quality-control standards, see 21 U.S.C. 353a(b)(1)(A) and (B) (Supp. V 1999); (3) the compounded product may not be a drug product identified by regulation as presenting difficulties for compounding that would adversely affect safety or efficacy, see 21 U.S.C. 353a(b)(3)(A) (Supp. V 1999); (4) the compounding may not produce a drug that has been withdrawn from the market for safety reasons, see 21 U.S.C. 353a(b)(1)(C) (Supp. V 1999); and (5) the pharmacist may not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product, see 21 U.S.C. 353a(b)(1)(D), 353a(b)(2) (Supp. V 1999). FDAMA also limits the total volume of compounded drug products that a pharmacy may

distribute out of State. See 21 U.S.C. 353a(b)(3)(B) (Supp. V 1999).

In addition, FDAMA makes the exemption of compounded drugs from the specified FDCA requirements contingent upon the pharmacy's compliance with limitations on advertising and promotion of compounded drug products. Section 353a(a) exempts pharmacy compounding from the new drug approval and other requirements only if the compounded drug is produced "based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. 353a(a) (Supp. V 1999). Section 353a(c) further provides that a pharmacy is entitled to the exemption only if it "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug." 21 U.S.C. 353a(c) (Supp. V 1999). The advertising limitation does not, however, prevent the pharmacy from advertising that it performs compounding services generally. 21 U.S.C. 353a(c) (Supp. V 1999).

3. In November 1998, shortly before the relevant provisions of FDAMA took effect, respondent pharmacies, which regularly compound drugs in significant quantities, commenced this suit in the United States District Court for the District of Nevada against the Secretary of Health and Human Services and the Commissioner of the FDA. Respondents sought a declaratory judgment that Sections 353a(a) and (c) violate the First Amendment and an order enjoining enforcement of those provisions against them.

The district court initially granted respondents a temporary restraining order that enjoined the government from enforcing Section 353a(c). Pet. App. 60a-70a. The parties subsequently filed cross-motions for summary judgment. The district court, concluding that Sections 353a(a) and (c) violate the First Amendment, granted respondents' motion, denied the government's motion, and permanently enjoined the FDA from enforcing the solicitation and advertising restrictions in Sections 353a(a) and (c). Pet. App. 16a-57a. The court further held that the restrictions were severable from the remainder of Section 353a. Id. at 57a-59a.

4. The United States Court of Appeals for the Ninth Circuit affirmed in part and reversed in part. Pet. App. 1a-15a.

a. Applying the four-part test enunciated in Central Hudson Gas & Electric Corp. v. Public Service Commission, 447 U.S. 557 (1980), for determining the constitutionality of regulation of commercial speech, the court of appeals affirmed the district court's holding that Sections 353a(a) and (c) violate the First Amendment. Pet. App. 4a-12a.

Because the government did not contest that the advertising and solicitation limitations in Section 353a apply to lawful, non-misleading speech, the court of appeals began its analysis with the second element in the Central Hudson analysis -- whether the governmental interests that underlie Section 353a's solicitation and advertising conditions are substantial. Pet. App. 5a. The court recognized that the government has substantial interests in

"protecting the public health and safety" and "preserving the integrity of the drug approval process." Pet. App. 5a. The court also recognized that "[t]he government's effort to balance competing goals can be a substantial interest." Id. at 6a. The court concluded, however, that the government had not demonstrated that "its interest in striking a balance between ensuring compounding availability and limiting widespread compounding is substantial." Id. at 7a. The court reached that conclusion because, in its view, "[t]here is insufficient evidence in the record to conclude that the government has a substantial interest in preventing widespread compounding." Ibid.

Turning to the third step in the Central Hudson analysis, the court held that the solicitation and advertising limitations in Section 353a do not directly advance either of the asserted interests that the court did find to be substantial -- protecting the public health and safety and preserving the integrity of the new drug approval process. Pet. App. 7a-10a. The court reasoned that the government "has not offered evidence or arguments to explain sufficiently why such restrictions will reduce the type of consumption of compounded drugs that is harmful, and even admits that it has a substantial interest in ensuring the availability of compounded drugs." Id. at 7a-8a. The court also concluded that, "[w]ithout the advertising restrictions, other safeguards exist to protect the public." Id. at 8a (citing 21 U.S.C. 353a(a) (requiring valid prescription for compounded drug products), 353a(b)(1) (limiting substances that pharmacists may use in

compounded products), and 353a(b)(1)(D) (Supp. V 1999) (preventing pharmacists from regularly compounding drugs that are essentially copies of commercially available products)).

In addition, relying on Rubin v. Coors Brewing Co., 514 U.S. 476 (1995), and Greater New Orleans Broadcasting Ass'n v. United States, 527 U.S. 173 (1999), the court concluded that Section 353a "is so riddled with exceptions that it is unlikely that the speech restrictions would actually succeed in depressing the volume of compounded drugs." Pet. App. 9a. The court observed that "pharmacists can advertise their compounding services and promote their skills at medical trade events so long as they do not promote the compounding of any particular drug," and that a pharmacist may call a physician and recommend a compounded drug if a patient comes in with a prescription for a commercial drug and provides information to the pharmacist that indicates that the patient might require a compounded product. Ibid. In addition, the court stated that FDAMA permits compounded drugs to constitute 5% of the total interstate distributions and 100% of the total intrastate distributions by a particular pharmacy. Ibid. (citing 21 U.S.C. 353a(b)(3) (Supp. V 1999)).

The court next addressed the fourth Central Hudson factor and concluded that the advertising and solicitation restrictions "are more extensive than necessary to achieve the asserted government interest." Pet. App. 10a. The court suggested that, instead of limiting advertising, the FDA could require disclaimers stating that the compounded drugs being advertised had not been subjected

to the FDA's approval process. Ibid. The court also offered the alternative of requiring all compounded drugs, including those created on an individual basis as part of the traditional practice of pharmacy, to undergo the safety and effectiveness testing required for new drugs under the FDCA. Ibid. The court rejected the government's argument that those alternatives would not address the government's interest in drawing a workable distinction between traditional, patient-based compounding and the manufacturing of new drugs, because the court had already determined that the government's interest in balancing those competing goals is not substantial. Id. at 11a.

b. Although the court of appeals affirmed the district court's judgment insofar as it held that the solicitation and advertising conditions in Section 353a violate the First Amendment, the court, accepting the government's submission, reversed the district court's decision to sever those provisions from the rest of Section 353a. Pet. App. 12a-15a. The court reasoned that "Congress intended to provide access to compounded drugs while preventing pharmacies from making an end run around the FDA's drug manufacturing requirements." Id. at 12a. Because "Congress meant to exempt compounding pharmacists from FDCA requirements only in return for a prohibition on the promotion of specific compounded drugs," the court concluded that the solicitation and advertising restrictions could not be severed from the rest of Section 353a. Id. at 13a-14a. Accordingly, the court invalidated Section 353a in its entirety. Id. at 15a.

SUMMARY OF ARGUMENT

A. Section 353a attempts to achieve two important but competing goals. It seeks to preserve the integrity of the FDCA's new drug approval process, which protects the public health by ensuring that new drugs are not widely distributed in interstate commerce unless they are first proven safe and effective. It also seeks to preserve the availability of compounded drugs for those individual patients who, for particularized medical reasons, cannot use commercial products that have been approved by the FDA.

Based on its long experience with the regulation of drugs, Congress concluded that proof of the safety and effectiveness of a new drug must be established by rigorous, scientifically valid studies rather than the impressions of individual doctors, who cannot by themselves compile and master the necessary information. Historical experience also convinced Congress that a premarket approval requirement is necessary to ensure that those who promote and distribute new drugs, and realize profits from their distribution, undertake the investigations necessary to establish safety and effectiveness.

At the same time, Congress recognized that it is also important to ensure that safe and effective drug treatments are in fact available, and that goal is also reflected in the FDCA. Consistent with that goal, the FDA historically refrained from enforcing the new drug approval requirements against pharmacies that compounded drugs in response to valid prescriptions to meet the medical needs of individual patients. That policy recognized

that compounding in response to individual medical needs is a traditional element of the practice of pharmacy that may have important health benefits, but pharmacies often will be unable to bear the burden and expense necessary to demonstrate to the FDA the safety and effectiveness of the compounded drugs before they are sold because of the limited market for them.

Experience showed, however, that some compounding was being conducted in a manner that threatened the safeguarding function of the new drug approval process. Some pharmacies were compounding outside the scope of normal pharmacy practice and mass-producing and distributing compounded drugs in a manner tantamount to the manufacture of new drugs. Compounding on that scale exposed significant numbers of people to the health and safety risks that had prompted enactment of the new drug approval requirements in the first place. Moreover, such compounding threatened the integrity and efficacy of the new drug approval process by making it less likely that manufacturers would have the requisite incentive to demonstrate that their new drugs are safe and effective for their intended uses. Pharmacies could mass-produce a particular drug product, stimulate demand for the product through soliciting and advertising, and thereby effectively manufacture and introduce the drug into interstate commerce without complying with the approval requirements. That practice would significantly reduce the incentives of manufacturers to bear the cost of establishing that the drugs they seek to market are safe and effective, because a manufacturer could obtain a pharmacy license and establish a

pharmacy entity to mass-produce drugs through compounding and thus circumvent the premarket approval requirements. Before enactment of Section 353a, the FDA therefore took enforcement actions against pharmacies that were manufacturing under the guise of compounding.

When Congress enacted Section 353a, it sought to achieve essentially the same balance of interests that the FDA had pursued through its enforcement policy - ensuring the continued availability of compounding to address the particularized needs of individual patients in cases in which it would be impractical to require a demonstration to the FDA of safety and effectiveness, while limiting the scope of compounding to prevent unregulated manufacturing that would threaten the integrity of the premarket approval process and undermine the FDCA regulatory scheme. Congress's effort to balance those two independently compelling but competing interests is itself a substantial governmental interest.

B. Section 353a directly and materially advances that substantial interest. Under certain conditions, Section 353a exempts compounded products from the FDCA's provisions governing new drug approval, good manufacturing practice, and adequate directions for use. The conditions at issue here are the limitations on the solicitation of prescriptions for and advertising of particular compounded drugs. Although those conditions restrict promotion of particular drugs, they do not restrict promotion of the compounding service in any other way. The specific solicitation and advertising conditions advance the government's interest because promotion of particular drugs

reasonably distinguishes drug manufacturing that should be subject to the premarket approval process from compounding in response to individual medical needs.

Traditional compounding involves the provision of a service in response to a physician's prescription and an individual patient's particular medical needs. Advertising the specific products created in the provision of that service (as opposed to advertising the compounding service itself) is not necessary to or characteristic of traditional compounding by a pharmacy. Drug manufacturing, in contrast, is the mass production of a homogenized product, typically for a substantial market, and advertising of particular drugs is typically a critical component of a successful manufacturing business. Restricting the compounding exemption to compounded products that are not subject to promotional activities characteristic of manufacturing ensures that the exemption does not create a loophole that would undermine the new drug approval process.

Limiting the exemption from the regulatory approval process to compounded drugs that are not advertised also reflects Congress's judgment in enacting the FDCA that the public health is best served when those who develop, distribute, and promote new drugs prove that those drugs are safe and effective. By preventing circumvention of the new drug approval requirements, the promotion limitations preserve the incentives for drug manufacturers to undertake the studies necessary to demonstrate that new drugs are safe and effective. Conditioning the exemption from the drug

approval requirements on whether a compounder promotes particular drugs is also consistent with the role that advertising and other promotional material have long played in determining the scope of regulation under the FDCA. For example, promotional activity has been an important consideration by the FDA in determining both whether a particular product is a drug subject to regulation under the FDCA and whether a new drug or a supplemental new drug application is required for a particular drug product.

The court of appeals therefore erred in concluding that the advertising and solicitation conditions on the availability of the exemption under Section 353a do not advance the government's interests. The other conditions on the availability of the exemption do not, as the court believed, provide adequate safeguards to protect the public. Nor do other provisions in Section 353a undermine the effectiveness of the advertising and solicitation limitations. Indeed, those provisions serve different purposes and ensure that the limitations are appropriately tailored to the government's interests.

C. The advertising and solicitation conditions on the availability of the exemption under Section 353a are carefully crafted so as to be no more extensive than necessary to advance the government's goals. They do not impose a prohibition on speech: a pharmacy that wishes to mass-produce a particular drug product and promote that product by advertising or by soliciting prescriptions can do so by complying with the premarket approval requirements that apply to other drug manufacturers.

The conditions on the availability of the exemption are also tailored to accommodate commercial speech attendant to compounding within the traditional practice of pharmacy. Section 353a(c) permits a pharmacy to advertise and promote its general compounding services. That kind of advertising promotes the availability of compounding in response to individual medical needs and does not threaten the integrity of the new drug approval process. Section 353a(a) permits compounding in limited quantities in anticipation of a valid prescription when that compounding is based on an established relationship among the pharmacist, the practitioner and the patient. It also permits a pharmacist to call a physician and recommend a compounded drug if a patient seeks to fill a prescription for a commercial drug and provides information that leads the pharmacist to conclude that a compounded product is required. Both of those practices are consistent with traditional compounding by a pharmacy in response to particularized medical needs and do not compromise the new drug approval requirements.

Finally, the alternatives to the advertising and solicitation limitations suggested by the court of appeals would not advance, but would undermine, the government's interests. Permitting promotion of compounded drugs provided they include disclaimers indicating that they have not been subject to premarket approval by the FDA would undermine the premarket approval process and would be fundamentally inconsistent with the protective framework of the FDCA. The other alternative offered by the court of appeals -- requiring premarket approval for all compounded drugs, even those

customized to meet the medical needs of specific patients -- would eliminate the availability of those products because demand for them is not sufficient to support the costs of the premarket approval process.

ARGUMENT

FDAMA'S LIMITED EXEMPTION FROM THE NEW DRUG APPROVAL REQUIREMENTS FOR DRUGS COMPOUNDED BY PHARMACISTS WHO DO NOT SOLICIT PRESCRIPTIONS FOR OR ADVERTISE PARTICULAR COMPOUNDED DRUGS IS CONSISTENT WITH THE FIRST AMENDMENT

Since 1938, the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 et seq., has prohibited the introduction into interstate commerce of a new drug without prior approval of the Food and Drug Administration (FDA). 21 U.S.C. 355(a). In the Food and Drug Administration Modernization Act of 1997 (FDAMA), Congress provided a limited exemption from the new drug approval and certain related requirements of the FDCA for drugs compounded by pharmacists. See 21 U.S.C. 353a (Supp. V 1999). In this case, the United States Court of Appeals for the Ninth Circuit held that the solicitation and advertising limitations that Congress adopted as conditions on the availability of that exemption violate the First Amendment. Contrary to the Ninth Circuit's conclusion, the limitations on the exemption provided by Section 353a are fully consistent with the First Amendment.[1]

---

[1] The government agrees with the court of appeals' conclusion (Pet. App. 12a-15a) that, if the solicitation and advertising provisions in Sections 353a(a) and (c) are unconstitutional, they are not severable from the remainder of Section 353a. For that reason, the government did not seek this Court's review of the severability issue. Respondents did not raise the issue in their brief in opposition, and they did not file a cross-petition for a writ of certiorari on the issue. The severability question is

In Central Hudson Gas & Electric Corp. v. Public Service Commission, 447 U.S. 557 (1980), this Court enunciated a four-part inquiry to determine the constitutionality under the First Amendment of government regulation of commercial speech: first, whether the speech "accurately inform[s] the public about lawful [commercial] activity," id. at 563; second, "whether the asserted governmental interest [underlying the speech regulation] is substantial," id. at 566; third, "whether the regulation directly advances the governmental interest asserted," ibid.; and, finally, "whether it is not more extensive than is necessary to serve that interest" (ibid.).

With respect to the first part of the Central Hudson inquiry, the government assumes that respondents' advertisements would be accurate and concern an activity that is otherwise lawful under the carefully circumscribed exemption that Congress has established for compounding. It is important, however, to stress that this case, unlike most commercial speech cases, does not involve a restriction on advertising that has been imposed in connection with an activity that the government otherwise has declined to prohibit. Before 1997, the introduction of compounded new drugs into interstate commerce - like the introduction of all other unapproved new drugs - was unlawful in all circumstances. In enacting Section 353a, Congress created an exemption to that generally applicable prohibition on the distribution of new drugs, but conditioned that

---

therefore not before the Court. See, e.g., Bates v. United States, 522 U.S. 23, 32 n.7 (1997).

exemption on compliance with a number of requirements, including restrictions on solicitation and advertising. As the court of appeals explained, Congress "intended to provide access to compounded drugs while preventing pharmacies from making an end run around the FDA's drug manufacturing requirements." Pet. App. 12a. Congress therefore "meant to exempt compounding pharmacists from FDCA requirements only in return for a prohibition on the promotion of specific compounded drugs." Id. at 13a-14a. That is to say, but for the advertising restrictions in Section 353a, the relevant commercial conduct - the sale of new drugs that have not been shown to be safe and effective - would be (and is) prohibited.

Accordingly, this case is not one in which the government generally permits certain conduct and asserts a hypothetical (but uninvoked) "greater power" to prohibit the advertised conduct as a justification for exercising the "lesser power" of restricting the advertising of that conduct. See 44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484, 510-513 (1996) (plurality opinion). Instead, Congress has exercised the "greater power" to prohibit the distribution of unapproved new drugs, and has permitted an exception to that prohibition only on compliance with various conditions, including restrictions on the solicitation and advertising of that otherwise unlawful commercial activity. The question, then, is whether Congress's inclusion of limitations on solicitation and advertising among the conditions on the availability of the exemption from certain of the FDCA's requirements satisfies the remaining three Central Hudson factors.

A. Substantial Governmental Interests Underlie Section 353a

In enacting Section 353a, Congress attempted to balance two goals, each of which is substantial. First, Congress sought to preserve the effectiveness and integrity of the FDCA's new drug approval process and the protection of the public health that it provides. Second, Congress sought to preserve the availability of compounded drugs for those individual patients who, for particularized medical reasons, cannot use commercially available products that have been approved by the FDA. Achieving the proper balance between those two independently compelling but competing interests is itself a substantial governmental interest.

1. There is a substantial governmental interest in protecting the integrity of the FDCA's new drug approval process

As both Congress and this Court have recognized, the widespread distribution of drugs that have not been shown to be safe and effective poses significant health risks. See United States v. Rutherford, 442 U.S. 544, 556-557 (1979); Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609, 622 (1973). The FDCA's new drug approval process is the culmination of a century of congressional efforts to advance the substantial interest in preventing those risks.

In the 19th century, the United States, which lacked laws and regulations of the sort that were in place in European countries, was plagued by substandard and contaminated drugs. Injuries from such drugs, such as a contaminated diphtheria vaccine that caused the death of a dozen children in 1902, eventually led to enactment of the Pure Food and Drugs Act of 1906, ch. 3915, 34 Stat. 768,

which prohibited interstate shipment of adulterated or misbranded drugs. See W.F. Janssen, Outline of the History of U.S. Drug Regulation and Labeling, 36 Food, Drug & Cosm. L.J. 420, 422-425 (1981). The 1906 Act, however, proved insufficient to ensure that marketed drugs were safe for use. Perhaps the most notorious example of that insufficiency was the Elixir Sulfanilamide tragedy of 1937. A company that had marketed sulfanilamide in capsule and tablet form began marketing the drug in a liquid form without adequately testing the safety of the liquid in which the sulfanilamide was dissolved. Before the drug could be recalled, 107 people, mostly children, died from using the product. See Elixir Sulfanilamide, S. Doc. 124, 75th Cong., 2d Session (1937); V. Henry, Problems with Pharmaceutical Regulation in the United States, 14 J. Leg. Med. 617, 619 (1993).

Congress enacted the FDCA in 1938 based on the historical experience demonstrating that manufacturer self-interest and physician screening were insufficient to protect the public from the dangers of widespread distribution of unsafe drugs. See Act of June 25, 1938, ch. 675, 52 Stat. 1040. At the heart of the new law was the new drug approval requirement -- that the manufacturer or distributor of a new drug must obtain approval from the FDA before introducing the new drug into interstate commerce. § 505(a), 52 Stat. 1052 (now codified as amended at 21 U.S.C. 355(a)).

Further experience revealed, however, that the preapproval requirements in the 1938 Act were still not sufficient to protect the public health and safety. One problem was that the Act

required proof only that a new drug was safe for its intended uses and not that it was effective for those uses. As a result, the FDA was forced to approve many drugs for general distribution even when there was no evidence that they would produce the therapeutic benefits claimed by their manufacturers. See S. Rep. No. 1744, 87th Cong., 2d Sess. Pt. 1, at 15-16 (1962); Drug Industry Antitrust Act: Hearings on S. 1552 Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary, Pt. 5, 87th Cong., 1st Sess. 2583-2585 (1961) (testimony of Abraham Ribicoff, Secretary of Health, Education, and Welfare). Because hundreds of new drugs were introduced each year, and information about their effectiveness took considerable time to develop and (when published at all) was scattered among hundreds of medical journals, physicians were unable to ascertain whether the drugs they were prescribing were effective. See S. Rep. No. 1744, supra, Pt. 1, at 37 (views of Sens. Kefauver, Carroll, Dodd, Hart, and Long); S. Rep. No. 448, 87th Cong., 1st Sess. 171 (1961); 108 Cong. Rec. 19,925-19,926 (1962); Warner-Lambert Co. v. Heckler, 787 F.2d 147, 156 (3d Cir. 1986). Prescription of ineffective drugs could have serious harmful consequences because, when an ineffective drug was prescribed, it usually replaced an older but effective drug. See S. Rep. No. 1744, supra, Pt. 1, at 37; see also Rutherford, 442 U.S. at 556-557 & n.13 (discussing danger that patients who use ineffective drugs will, as a consequence, delay or forgo use of effective drugs or other treatment).

Another problem with the 1938 Act was that a new drug application became effective automatically after 180 days if the FDA took no action. See S. Rep. No. 1744, supra, Pt. 1, at 40. Because of the automatic approval provision and the lack of independent and objective clinical studies to guide FDA physicians in evaluating new drugs, many drugs were released for distribution that were subsequently revealed to have serious (and sometimes deadly) side effects. See id. at 43. The possible dangers of automatic approval were graphically illustrat the thalidomide experience, in which reports of serious birth defe caused by the use of thalidomide in Europe surfaced shortly before he automatic approval requirement might have forced the FDA to permit widespread distribution of the drug in the United States. See id. at 40-43.

The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780, addressed those problems by strengthening the new drug approval process. The amendments eliminated the automatic approval provision and required manufacturers and distributors to demonstrate not only the safety but also the effectiveness of new drugs. Under the amended provisions, a new drug may not be introduced (or delivered for introduction) into interstate commerce until the manufacturer or distributor obtains the FDA's affirmative approval by establishing that the drug is safe and effective for each of its intended uses. See 21 U.S.C. 321(p), 331(d), 355(a)-(d); S. Rep. 1744, 87th Cong., 2d Sess. Pt. 2, at 4-5 (1962); 108 Cong. Rec. 17,366 (1962) (statement of Sen. Eastland).

The new drug approval requirements in effect today thus reflect two related and reasonable conclusions that Congress and the FDA drew from long experience with drug regulation. First, proof of the safety and effectiveness of a new drug must be established by rigorous, scientifically valid clinical studies rather than the impressions of individual doctors, who cannot by themselves compile and master the necessary information; and, second, a premarket approval requirement is necessary to ensure that those who promote and distribute new drugs, and seek to realize profits from their distribution, undertake the investigations necessary to establish effectiveness and safety. See Hynson, Westcott & Dunning, 412 U.S. at 619, 629-630; Warner-Lambert Co., 787 F.2d at 156. For these reasons, the new drug approval process is a critical component of the FDCA's regulatory framework for the protection of the public health and safety. As the district court and court of appeals both concluded (Pet. App. 5a-6a, 40a-41a), there is a substantial governmental interest in preserving the integrity of that process.

2. There is a substantial governmental interest in ensuring the availability of compounding in response to individual medical needs

At the same time that Congress sought, through the new drug approval process, to protect the public from unsafe and ineffective drugs, Congress recognized that it is also important to ensure that drug treatments that are safe and effective are in fact available. Congress therefore carefully crafted the new drug approval process "to insure that governmental control does not become so rigid that

the flow of new drugs to the market, and the incentive to undergo the expense involved in preparing them for the market, become stifled." S. Rep. No. 1744, supra, Pt. 1, at 14-15; see id. at 16; H.R. Rep. No. 2139, 75th Cong., 3d Sess. 823 (1938); Hynson, Westcott & Dunning, 412 U.S. at 639 n.2 (Powell, J., concurring) (noting the public interest "in protecting the drugs that are useful in the prevention, control, or treatment of illness").

Congress also has generally refrained from providing in the FDCA for the FDA to limit a physician, as part of the practice of medicine, from prescribing any legally available product for a particular patient. See 37 Fed. Reg. 16,503 (1972) (noting repeated references in the legislative history of the 1938 Act and the 1962 amendments that Congress did not intend the FDA to interfere with a physician's ability to prescribe legally approved products for unapproved uses); e.g., S. Rep. No. 361, 74th Cong., 1st Sess. 3 (1935); H.R. Rep. No. 2755, 74th Cong., 2d Sess. 5 (1936); S. Rep. No. 1744, supra, Pt. 1, at 56 (views of Sens. Dirksen and Hruska). Consistent with that background, the FDA has permitted physicians to prescribe approved drugs for uses that are not identified in approved labeling. See 12 FDA Drug Bulletin 4-5 (1982); J.M. Beck & E.D. Azari, FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions, 53 Food, Drug, & Cosm. L.J. 71, 76-79 (1998). That policy reflects the FDA's recognition that certain off-label uses perform an important therapeutic role in certain areas of medical practice, and that undue restrictions on such uses could have adverse health consequences. See id., at

79-80; cf. Buckman Co. v. Plaintiffs' Legal Comm., 121 S. Ct. 1012, 1018-1019 & n.5 (2001) (discussing off-label uses prescribed or administered by physicians in the context of the FDCA's device provisions). The FDA has followed that policy even though manufacturers and distributors may not distribute approved products for off-label uses -- and therefore may not promote off-label uses -- without first demonstrating to the FDA that the products are safe and effective for those uses and obtaining FDA approval. 12 FDA Drug Bulletin 4, 5.

Similar considerations led the FDA to refrain from taking enforcement action against pharmacists who compounded drugs in response to valid prescriptions to meet the medical needs of individual patients, as determined by their physicians, even though introduction of compounded drugs into interstate commerce without FDA approval was illegal before enactment of Section 353a in 1977. See pp. __, supra. The FDA recognized that compounding in response to a valid prescription to meet individual medical needs is a traditional element of the practice of pharmacy. Pet. App. 71a; see also L.V. Allen, Jr., The Art, Science, and Technology of Pharmaceutical Compounding xvi, 1 (1998); C.M. Wyandt & J.S. Williamson, Compounding: Regulatory and Management Issues, Drug Topics, July 1999, at 43.[2]

[2] See also Virginia State Bd. of Pharm. v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, 752, 766 (1976) (noting that, in the mid-1970s, approximately 5% of prescriptions were compounded by pharmacists); S.H. Kalman & J.F. Schlegel, Standards of Practice for the Profession of Pharmacy, NS19 No. 3 American Pharmacy 29 (1979) (discussing pharmacists' compounding responsibilities); Complaint ¶ 20 reprinted in C.A. Excerpts of Record (hereinafter C.A. E.R.) 5 ("Pharmacy compounding is a time-honored, customary and traditional part of pharmacy practice. It is a mandatory subject in most pharmacy schools. Most, if not all, state laws require that pharmacists be proficient in compounding and that they maintain special compounding equipment.").

Like certain off-label uses, compounding in response to individual medical needs may have important health benefits. It allows physicians and pharmacists to work together to develop customized therapies for patients for whom commercially manufactured drugs are not suitable for various medical reasons. For example, when a patient has an allergy to a component of a commercially available product, or an approved drug does not come in a dosage appropriate for an individual or in a delivery system that the patient can tolerate, the physician and pharmacist can work together to create a compounded product that addresses the patient's particularized needs. See Professionals & Patients for Customized Care v. Shalala, 56 F.3d 592, 593 (5th Cir. 1995); Pet. App. 41a-42a.[3]

Of course, it might theoretically be ideal if a pharmacy first demonstrated to the FDA that a compounded drug is safe and effective for its intended use before it is sold to an individual

[3] See also C.A. E.R. 6 (giving examples of the benefits of compounding); K. Ranelli, Extending the Family, The Hartford Courant, Mar. 16, 2000, at E1 ("Compounding can include making a natural, bio-identical drug for hormone therapy, changing an oral medication into a topical cream for patients who can't swallow easily, and tailoring drugs to children's taste by adding a fruit extract."); H. Dukes, Compounding of Medications Enjoys a Comeback, South Bend Tribune, Jan. 31, 2001, at C1 (benefits of compounding include pediatric dosages of drugs manufactured only for adults and providing medications that drug companies no longer make).

patient. However, because obtaining FDA approval of a new drug is a costly process, requiring FDA approval of all drug products compounded by pharmacies for the particular needs of an individual patient would, as a practical matter, eliminate the practice of compounding, and thereby eliminate availability of compounded drugs for those patients who have no alternative treatment. The cost of developing and obtaining approval of a new drug that is not closely similar to an already approved drug is generally estimated to exceed $200 million dollars. See Henry, supra, at 617; J.A. Henderson, Jr. & A.D. Twerski, Drug Designs Are Different, 111 Yale L.J. 151, 164-165 (2001). The cost of developing drugs that closely resemble approved products is still substantial -- ranging from $300,000 to $500,000. See Balaji K., Generics: The Opportunity Beckons (July 2001) <http://www.inpharm.com/intelligence/frost010701.html>.

Just as those costs have discouraged manufacturers from developing drugs to treat rare illnesses, see Henry, supra, at 628-630, the high costs of the approval process would make it uneconomical for a typical pharmacist to obtain approval for a drug that is compounded for a limited number of people - sometimes only a single individual - for whom the product is medically necessary. Requiring approval in those circumstances would not be feasible, and advance approval of such individual compounded drugs is less central to protecting the broader public health than is the advance approval of products that are distributed more widely to the public. The FDA's policy of not enforcing the new drug approval

requirements against traditional pharmaceutical compounding was thus a reasonable exercise of informed regulatory enforcement discretion based on the conclusion that there is a substantial governmental interest in permitting compounding in response to the particularized medical needs of identified individuals -- a conclusion with which the district court and court of appeals in this case did not disagree (Pet. App. 7a-8a, 42a).

3. There is a substantial governmental interest in balancing the interests in permitting compounding in response to individual medical needs and protecting the integrity of the new drug approval process

a. Although there are benefits from drug compounding in appropriate individualized circumstances, experience under the FDA's enforcement policy prior to 1997 showed that compounding can also present significant health and safety risks. Some pharmacies were compounding outside the scope of normal pharmacy practice and were mass-producing and distributing compounded drugs in a manner tantamount to the manufacture of new drugs. Pet. App. 72a. Compounding on that scale exposed substantial numbers of the public to the kinds of risks that had led to the enactment of the new drug approval process in the first place. For example, some drug products compounded by pharmacies contained impurities that caused serious injuries, such as eye infections that required removal of patients' eyes, and fatalities, including deaths of infants. Id. at 73a; T. Nordenberg, Pharmacy Compounding: Customizing Prescription Drugs, 34 FDA Consumer No. 4, at 11 (2000); C.E. Myers, Needed: Serious Attention to Sterile Products, 53 Am. J. Health Sys. Pharm. 2582 (1996).

Even more significantly, compounding on a scale tantamount to manufacturing was allowing wholesale circumvention of the new drug approval process. Pet. App. 73a-74a. Pharmacies could mass-produce a particular drug product, stimulate demand for the product through advertising, and thereby effectively manufacture and distribute the drug in interstate commerce without complying with the new drug approval requirements. See FDA Reform Legislation: Hearings Before the Subcomm. on Health and the Env't of the House Comm. on Commerce, 104th Cong., 2d Sess. 31, 125 (1996) (FDAMA Hearings) (testimony of Hon. David A. Kessler, Commissioner, FDA); id. at 59 (FDA Analysis); Addressing the FDA's Performance, Efficiency, and Use of Resources: Hearings Before the Senate Comm. on Labor and Human Resources, 105th Cong., 1st Sess. 28 (1997) (testimony of Michael D. Friedman, M.D., and William Schultz, Deputy Commissioners, FDA).

That practice presented far more serious potential consequences than the possibility that small quantities of drugs that might be unsafe or ineffective might be sold by a local pharmacy in individual situations. The practice threatened to undermine the new drug approval process and weaken the very core mission of the FDCA itself. If drug producers could mass-produce drugs through pharmacy entities engaged in widespread compounding, and thus bypass the approval process, manufacturers would have far less incentive to bear the cost of establishing that the drugs they seek to market are in fact safe and effective. See FDAMA Hearings 31, 59; see also D.B. Brushwood, Responsive Regulation of Internet

Pharmacy Practice, 10 Annals Health L. 75, 85-86 (2001) (describing high-volume compounding that occurred in the 1990s as an "unregulated industry of clandestine drug manufacturers"). Cf. Weinberger v. Bentex Pharm., Inc., 412 U.S. 645, 653 (1973) (noting that it would be "inherently unfair" to require compliance by one manufacturer with the new drug approval requirements "while his competitors marketing similar drugs remain free to violate the Act").[4]

Because the FDA recognized the importance of balancing the interest in permitting compounding to meet individual medical needs with the interest in protecting the integrity of the new drug approval process, the FDA, before the enactment of Section 353a in 1997, brought enforcement actions against pharmacies that were engaged in compounding that was tantamount to manufacturing. Pet. App. 73a-74a; see pp. __, supra. When Congress addressed the compounding issue by enacting Section 353a, it sought to achieve essentially the same balance of interests that the FDA had pursued through its enforcement policy. See H.R. Conf. No. 399, 105th Cong., 1st Sess. Rep. 94 (1997) (explaining that Section 353a

---

[4] Attempts by drug manufacturers to bypass the new drug approval process are not infrequent. See, e.g., United States v. Sage Pharm., Inc., 210 F.3d 475 (5th Cir. 2000); Florida Breckenridge, Inc. v. Solvay Pharm., Inc., No. 98-4606 (11th Cir. May 11, 1999); United States v. Hiland, 909 F.2d 1114 (8th Cir. 1990); United States v. 50 Boxes More or Less, 909 F.2d 24 (1st Cir. 1990); United States v. Sandoz Pharm. Corp., 894 F.2d 825 (6th Cir. 1990); United States v. 225 Cartons, More or Less, of an Article or Drug, 871 F.2d 409 (3d Cir. 1989); United States v. Atropine Sulfate 1.0 Mg. (Article of Drug) Dey-Dose, 843 F.2d 860 (5th Cir. 1988); United States v. Articles of Drug, 826 F.2d 564 (7th Cir. 1987); Premo Pharm., Inc. v. United States, 629 F.2d 795 (2d Cir. 1980).

"ensure[s] continued availability of compounded drug products as a component of individualized therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding"); accord S. Rep. No. 43, 105th Cong., 1st Sess. 67 (1997).

b. The court of appeals refused to credit the government's interest in achieving that balance because, in the court's view, the government did not present "convincing evidence" of "the health risks associated with large numbers of patients taking [compounded] drugs." Pet. App. 6a-7a. That evidentiary demand was wholly misplaced. In the first place, this Court has made clear that the government may "justify [advertising and solicitation] restrictions based solely on history, consensus, and 'simple common sense.'" Lorillard Tobacco Co. v. Reilly, 121 S. Ct. 2404, 2422 (2001) (quoting Florida Bar v. Went For It, Inc., 515 U.S. 618, 628 (1995) (citations and internal quotation marks omitted)). As described above, the substantiality of the government's interests here is amply supported by the history of congressional regulation of drug manufacturing, the FDA's regulatory experience with compounding, and "simple common sense." Ibid.

Furthermore, the court of appeals' insistence that the government produce "convincing evidence" in court was particularly inappropriate in this case, because it was based on a rejection of the fundamental premises of the FDCA itself, which in turn reflect decades of agency and congressional experience -- that the widespread distribution of drugs that have not been shown to be

safe and effective poses substantial health risks, and that the FDCA's new drug approval requirements are a legitimate and effective means to address those risks. This Court has acknowledged the validity of those premises, see Rutherford, 442 U.S. at 556-557; Hynson, Westcott & Dunning, 412 U.S. at 619, 622, and the court of appeals had no basis to question them.

The court of appeals' ruling on this point appears to have stemmed from its failure to appreciate the full extent of the government's interest. That interest is not simply, as the court of appeals characterized it, in "preventing widespread compounding." Pet. App. 7a. Rather, as described above, the government's interest is in preventing compounding that is tantamount to manufacturing and therefore undermines the federal scheme for ensuring that drugs are safe and effective before they are introduced into commerce. Congress sought to balance that substantial interest with the substantial but competing interest in making compounded drug products available in circumstances in which they are necessary to meet the particularized medical needs of individual patients and a prior approval requirement generally would not be feasible. See H.R. Conf. Rep. No. 399, supra, at 94; S. Rep. No. 43, supra, at 67; compare Buckman Co., 121 S. Ct. at 1018 (under the FDCA, "the FDA pursues difficult (and often competing) objectives"). Balancing those two goals is a substantial governmental interest in its own right. See United States v. Edge Broad. Co., 509 U.S. 418, 428 (1993) (balancing

competing governmental concerns can be a substantial governmental interest for purposes of the Central Hudson test).

B. Section 353a Directly And Materially Advances The Government's Interests

Although Section 353a seeks to advance the same interests that the FDA previously pursued through the exercise of its enforcement discretion, Congress chose to endorse and lend the strength of its backing to those goals by setting forth in the FDCA itself the "parameters under which compounding is appropriate and lawful." S. Rep. No. 43, supra, at 67. Section 353a thus exempts compounded drug products from the FDCA's provisions governing new drug approval, as well as the provisions concerning good manufacturing practice and adequate directions for use, under certain specified conditions.

The conditions at issue here involve limitations on the solicitation of prescriptions and advertising. Section 353a(a) exempts compounding from the new drug approval and related requirements only if the compounded drug is produced "based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. 353a(a) (Supp. V 1999). Section 353a(c) further provides that a pharmacy is entitled to the exemption only if it "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug." 21 U.S.C. 353a(c) (Supp. V 1999). The advertising limitation does not, however, prevent the pharmacy from advertising that it performs compounding services generally. 21

U.S.C. 353a(c) (Supp. V 1999). The solicitation and advertising conditions on the application of the exemption directly and materially advance the government's interest in balancing the competing goals of ensuring the availability of compounding in response to particularized medical needs of individual patients and protecting the integrity of the new drug approval requirements.

1. Promotion of particular drugs reasonably distinguishes drug manufacturing that is subject to the premarket approval process from compounding in response to individual medical needs

a. Before enactment of Section 353a, the FDA considered a variety of factors to determine whether a pharmacy was manufacturing under the guise of compounding and thus circumventing the new drug approval requirements in a manner that materially undermined the purposes of the FDCA. See pp. __, supra; Pet. App. 76a-77a. Among those factors was whether the pharmacy was "[s]oliciting business (e.g., promoting, advertising, or using sales persons) to compound specific drug products, product classes, or therapeutic classes of drug products." Id. at 76a. The FDA explained that, in its experience, such practices "are far more consistent with those of drug manufacturers and wholesalers than with retail pharmacies." Id. at 72a. Building on the FDA's experience, Congress found similar considerations useful and appropriate in drawing the line between traditional, individualized compounding and compounding that is tantamount to manufacturing. See 143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997) (statement of Sen. Kennedy); ibid. (statement of Sen. Hutchinson).

As the FDA had previously determined, Congress reasonably concluded that advertising of particular drug products is a business practice that is characteristic of manufacturing but not of traditional compounding by a pharmacy for an individualized need. Traditional compounding involves the provision of a service in response to a physician's prescription and an individual patient's particular medical situation. See Pet. App. 71a-72a; Allen, supra, at xv, 1 (National Association of Boards of Pharmacy defines compounding as the preparation of a drug "as the result of a practitioner's Prescription Drug Order or initiative based on the pharmacist/patient/prescriber relationship."); Wyandt & Williamson, supra, at 43, 49 (same). Compounding is thus responsive: it arises out of "specific practitioner/patient/pharmacist relationships" and "result[s]" from the "practitioner's [p]rescription * * * or initiative." Id. at 49 (emphasis added). Compounding in anticipation of prescription drug orders occurs only based on "routine, regularly observed patterns." Ibid.; Allen, supra, at xv, 1. Compounding produces a medication that is "customiz[ed]" for "the patient's unique needs." A. Joyner, Local Pharmacies Invest In Compounding, Billings Gazette, Feb. 27, 2000, at 1D.[5]

[5] See Dukes, supra, at C1, C2 (describing compounding as providing "tailor-made" medicines); B.H. Thiers, Compounding Is Still Appropriate in Clinical Practice, 16 Dermatologic Clinic No. 2, at 330 (1998) (compounding "allows the physician to individualize treatment to the patient's specific needs"); Allen, supra, at xix (compounding involves providing "patient-specific products"); C.A. E.R. 5 ("It is common in the practice of compounding for a physician, pharmacist, and patient to collaborate to select the proper combination of ingredients, dosage, and method of application or ingestion.").

Advertising the particular products created in the provision of the compounding service (as opposed to advertising the compounding service itself) is not necessary to or characteristic of this type of responsive and customized service. Although advertising is useful in a broad market, it serves little purpose when a medication is compounded in response to an individual and often unique need.

Drug manufacturing is the large scale production of a drug product, typically for a substantial market. Promotion of the manufactured product to physicians or the public is a common feature of drug manufacturing. Pet. App. 72a; K.B. Leffler, Persuasion or Information? The Economics of Prescription Drug Advertising, 24 J.L. & Econ. 45, 46 (1981) (market for prescription drugs is "characterized by very large promotional expenditures"); National Institute for Health Care Management, Prescription Drugs and Mass Media Advertising, 2000, at 4 (Nov. 2001) <http://www.nihcm.org/DTCbrief2001.pdf> ($15.7 billion was spent on promotion of prescription drugs in 2000, including $4 billion for doctor's office detailing, $2.5 billion for direct advertisements to consumers, and almost $500 million for advertisements in medical journals). Successful competition in providing homogenous drug products "requires the identification and knowledge of individual manufacturers," and, thus, advertising typically is critical to successful drug manufacture. Leffler, supra, at 48 (explaining how centralized production of drugs increased the use of manufacturer trademarks and brand-name promotion); see E. Kremers & G. Urdang,

History of Pharmacy 164 (2d ed. 1951) (stating that the rise of the proprietary drug industry was "the product of the extension and perfection of the art of advertising, furthered by the trade-mark acts").[6] Expenditures on such advertising therefore are a fair proxy for actual or intended large-scale manufacturing. Thus, by restricting the compounding exemption to pharmacies that do not engage in the promotional conduct characteristic of manufacturing, Congress rationally calculated that "the exemption would not create a loophole that would allow unregulated drug manufacturing to occur under the guise of pharmacy compounding." 143 Cong. Rec. at S9839 (statement of Sen. Kennedy).

b. Conditioning exemption from the regulatory approval process for compounded drugs on the absence of promotion of those products also reflects the FDCA's underlying premise that the public health is best served when those who develop and promote new drugs prove that those drugs are safe and effective. See Hynson, Westcott & Dunning, 412 U.S. at 619, 629-630; pp. __, supra. If compounders could actively promote specific products through advertising without having to bear the costs of the new drug approval process, they would enjoy an unfair advantage over

[6] See also Allen, supra, at 1 (defining drug manufacturing to include "the promotion and marketing of [the manufactured] drugs"); Wyandt & Williamson, supra, at 6 (same); Administered Prices, Drugs, S. Rep. No. 448, supra, at 157 (noting that "virtually all who attempt to market some trademarked specialties engage in journal advertising, direct mail, and the supplying of free samples to physicians"); J. Avorn et al., Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians, 73 Am. J. of Med. 4, 7 (July 1982) (explaining that "[t]ypically, the initial promotion of a new drug is accompanied by extensive advertisement of its virtues").

traditional drug manufacturers, who must comply with the approval requirements. That unfair advantage would undermine the statutory incentive for drug manufacturers to comply with the approval requirements, which are the FDCA's central mechanism to ensure that drugs introduced into interstate commerce are safe and effective for their intended uses. See pp. __, supra (explaining that manufacturers could by-pass the approval process by establishing pharmacy subcomponents).

c. Advertising and other promotional material have long been critical factors in determining the scope of regulation under the FDCA. For example, the FDA considers labeling, promotional material, and advertising (among other things) to determine whether a substance constitutes a "drug" that is subject to regulation under the Act because it is intended to treat disease or otherwise to affect the structure or function of the body. See 21 U.S.C. 321(g)(1); e.g., United States v. Storage Spaces Designated Nos. "8" and "49" Located at 277 E. Douglas, Visalia, CA, 777 F.2d 1363, 1366-1367 & n.6 (9th Cir. 1985); National Nutritional Foods Ass'n v. Mathews, 557 F.2d 325, 334 (2d Cir. 1977); United States v. Article . . . Consisting of 216 Individually Cartoned Bottles, 409 F.2d 734, 739 (2d Cir. 1969) (collecting cases).

Similarly, promotional representations can be an important indicator of whether a new drug application or supplemental new drug application is required for a product, e.g., as a result of advertising recommending a new use for the product. The labeling for a drug must indicate "all conditions, purposes, or uses for

which such drug is intended, including conditions, purposes, or uses for which it is prescribed, recommended, or suggested in its oral, written, printed, or graphic advertising." 21 C.F.R. 201.5; see also 21 C.F.R. 201.128 (in determining a drug's intended uses, the FDA considers, among other things, "labeling claims, advertising matter, or oral or written statements" by the persons legally responsible for the product's labeling or their representatives). If a product is labeled for a new intended use, as required by those regulations, it is a "new drug" (for which FDA premarket approval is required), because it is not generally recognized to be safe and effective for use "under the conditions prescribed, recommended, or suggested in the labeling thereof," or, while so recognized, has not been used for a material time or to a material extent under such conditions. 21 U.S.C. 321(p); 108 Cong. Rec. at 17,366 (statement of Sen. Eastland). The use claimed for a drug in promotional material (and otherwise) thus may be an important factor in determining whether or not it is a new drug and whether FDA premarket approval is required. See S. Rep. No. 1744, supra, Pt. 1, at 17; id. at 59-60 (views of Sens. Dirksen and Sen. Hruska); S. Rep. No. 1744, supra, Pt. 2, at 5; see also Hynson, Westcott & Dunning, 412 U.S. at 613, 629, 632 (new drug is one not generally recognized by experts as safe and effective for its "intended use"). Therefore, denying the exemption from the FDA approval requirements when compounded drug products are advertised or otherwise promoted is entirely consistent with the overall structure and administrative implementation of the FDCA.

2. The court of appeals erred in concluding that the advertising and solicitation conditions do not materially advance the government's interests

a. The court of appeals erroneously concluded that limiting the exemption from the premarket approval and other requirements to pharmacies that do not promote particular compounded products does not directly and materially advance the government's interests. Pet. App. 7a-10a. As an initial matter, the court faulted the government for failing to demonstrate that Section "353a's speech restrictions will keep the demand for particular compounded drugs artificially low, and thereby protect unwary consumers." Id. at 8a. Once again, the court of appeals appears to have misunderstood the government's argument and burden. As discussed above, the government's argument is that Congress sensibly concluded that advertising for a particular compounded drug product reasonably identifies the point at which the interest in preserving the integrity of the new drug approval requirements outweighs the interest in protecting the availability of traditional pharmaceutical compounding in response to individual medical needs. That contention in no way requires a showing that Section 353a's speech restrictions will suppress the demand for particular compounded drugs.

The court of appeals also relied on its own assessment that other "safeguards exist to protect the public." Pet. App. 8a. The provisions of Section 353a to which the court referred, however, do not advance the governmental interests underlying that Section. For example, the court noted that, under FDAMA, "[n]o compounded

drug may be dispensed without a valid prescription from a licensed physician." Id. at 8a-9a (citing 21 U.S.C. 355a(a) (Supp. V 1999)). That requirement, however, is insufficient to advance the government's interest in preserving the integrity and safeguarding function of the FDCA's new drug approval process. That process rests on the learning accumulated over decades by the FDA and Congress that the ultimate determination whether a new drug is safe and effective cannot be left to individual doctors, who cannot by themselves compile and master the necessary information, but must be made by the FDA on the basis of scientific evidence submitted by the manufacturer. See Hynson, Westcott & Dunning, 412 U.S. at 619, 630; Warner-Lambert Co., 787 F.2d at 156.

The court of appeals also observed that a "pharmacist cannot regularly compound drugs that are essentially copies of a commercially available drug product." Pet. App. 9a (citing 21 U.S.C. 353a(b)(1)(D) (Supp. V 1999)). Although that limitation does indeed further the government's interest in preventing pharmacies from manufacturing products that are already available without complying with the FDCA's requirements, it does not address the problem of the manufacture through widespread compounding of products that are different from those that are commercially available. That latter form of compounding is addressed by Sections 353a(a) and (c), by ensuring that entities that promote the distribution in interstate commerce of new drug products comply, as must conventional manufacturers, with the new drug approval requirements. By requiring such parity in treatment,

Section 353a preserves the integrity and protective function of the new drug approval process and prevents the widespread distribution of new drugs that have not been proven safe and effective.

Nor do 21 U.S.C. 353a(b)(1)(A) and (B), which limit the substances that pharmacists may use in compounding, adequately address the governmental interest in preventing the manufacturing of new drugs under the guise of compounding. Those provisions require that the ingredients used in compounded products meet certain quality standards, which are less extensive than those that apply to approved products under 21 U.S.C. 351(a)(2)(B) (Supp. V 1999). They do not ensure the safety and effectiveness of the compounded drugs themselves, which are still unapproved new drugs; and they do not operate to prevent compounding activity that is on the scale and in the manner of manufacturing.

b. The Ninth Circuit also concluded that Section 353a fails the third Central Hudson inquiry because, in the court's view, it "is so riddled with exceptions that it is unlikely that the speech restrictions would actually succeed in depressing the volume of compounded drugs." Pet. App. 9a. The court noted, for example, that Section 353a permits pharmacies to advertise their general compounding services (see 21 U.S.C. 353a(c) (Supp. V 1999)) and does not prevent them from dispensing significant quantities of drugs intrastate (see 21 U.S.C. 353a(b)(3) (Supp. V 1999)). Those provisions, however, do not undermine the government's interest in preventing manufacturing under the guise of compounding.

As discussed above, if compounders could actively promote particular compounded drug products without complying with the new drug approval requirements, they would enjoy an unfair advantage over traditional drug manufacturers that would significantly reduce the incentives for manufacturers to expend the resources necessary to prove that their new drugs are safe and effective. Indeed, under such a regime, traditional drug manufacturers could establish compounding entities and circumvent the approval process.

Moreover, advertising of particular drug products is a historical and critical characteristic of drug manufacturing but not of traditional compounding. See pp. __, supra. General advertising that a pharmacy provides compounding services does not suggest the existence, or foster the growth, of a market for any particular compounded drug, and thus does not distort the incentives of drug manufacturers to comply with the new drug approval requirements. Permitting pharmacies to advertise that they provide compounding services therefore is consistent with, not at odds with, Congress's interest in ensuring that drugs are widely distributed in commerce only after they have been proven to be safe and effective for their intended uses. Allowing general advertising of compounding services -- including information about the pharmacist's experience, the timeliness of services, and physician satisfaction -- also promotes Congress's interest in preserving the availability of medically necessary treatments when demand is insufficient to justify the costs of pre-approval. Section 353a thus does not permit "speech that poses the same risks

the Government purports to fear." Greater New Orleans Broad., 527 U.S. at 195.

Nor does 21 U.S.C. 353a(b)(3) (Supp. V 1999) undermine the government's interest. Section 353a(b)(3) provides that a pharmacy may avail itself of the compounding exemption only if it is located in a State that has entered into an agreement with the Secretary that addresses the interstate distribution of inordinate amounts of compounded drugs, or if the pharmacy's total interstate distribution of compounded drug products does not exceed 5 percent of its total prescription orders. See 21 U.S.C. 353a(b)(3) (Supp. V 1999). That provision imposes a restraint in addition to and somewhat different in purpose from the restrictions on advertising and solicitation of prescriptions for individual drugs. The advertising and solicitation limitations prevent the manufacture of particular drug products under the guise of compounding. Section 353a(b)(3) limits the volume of the pharmacy's overall interstate sales of compounded drugs to ensure that the pharmacy retains its general character as a retail pharmacy rather than a drug manufacturer.

The volume limitation in Section 353a(b)(3) applies only to interstate distributions so that the States may continue to play their traditional role in regulating the practice of pharmacy. See 143 Cong. Rec. S12,242 (daily ed. Nov. 9, 1997) (statement of Sen. Jeffords) (Congress intended "to establish a rational framework for pharmacy compounding [that] respects the State regulation of pharmacy while allowing an appropriate role for the FDA"). The

absence of volume limitations on overall intrastate distributions does not, however, undermine the advertising and solicitation restrictions, which continue to prevent compounding of a particular drug that would be tantamount to the manufacturing of new drugs.

C. Section 353a Does Not Burden An Excessive Amount Of Speech In Relation To Its Purposes

The final consideration under Central Hudson is whether the advertising and solicitation limitations in Section 353a are "more extensive than * * * necessary" to serve the governmental interests that they advance. 447 U.S. at 566. As this Court recently reiterated, that inquiry is not a "least restrictive means" test. Lorillard Tobacco Co., 121 S. Ct. 2422 (2001) (quoting Went For It, 515 U.S. at 632). Instead, the First Amendment requires only a "reasonable 'fit between the legislature's ends and the means chosen to accomplish those ends.'" Ibid. (quoting in turn Board of Trs. of State Univ. of N.Y. v. Fox, 492 U.S. 469, 480 (1989)). The limitations in Section 353a satisfy that requirement.

1. The advertising and solicitation limitations are carefully crafted to meet the government's goals

The limitations on advertising and solicitation in Section 353a are not more extensive than necessary to advance the government's goals. Most significantly, Section 353a does not absolutely prohibit any speech. A pharmacy that wishes to mass-produce a particular drug product and promote that product by advertising or soliciting prescriptions can do so -- just as any other drug manufacturer can -- if it complies with the FDCA's new drug approval and related requirements. It is only if the pharmacy

desires to avail itself of the exemption from those otherwise generally applicable requirements on conduct that it must limit its promotional activities. As explained above, if a pharmacy could produce and promote compounded drugs without complying with the new drug approval requirements, the requirements would be substantially undermined. The limitation on promotion is thus well calibrated to the government's interest in protecting the integrity of the new drug approval requirements. Cf. Dolan v. City of Tigard, 512 U.S. 374, 385, 391 (1994) (government may condition a benefit on the relinquishment of a constitutional right if waiver of the right is reasonably related to the benefit) (citing Pickering v. Board of Educ., 391 U.S. 563, 568 (1968) (government may impose limitations on the speech of its employees when justified by its interests as an employer)).

The advertising limitation is also tailored to accommodate the commercial speech necessary to the practice of traditional compounding. Section 353a(c) expressly permits advertising for and promotion of "the compounding service provided by the licensed pharmacist." 21 U.S.C. 353a(c) (Supp. V 1999). Therefore, compounders may, consistent with FDAMA, advertise that they perform compounding services, that they are experts in compounding, and that they stand ready to fill prescriptions for compounded drug products. They may also advertise other information that relates to their general compounding practice, such as the mark-up that they charge in exchange for their compounding services. This kind of advertising is consistent with the government's interest under

FDAMA in ensuring the availability of compounding in response to individual medical needs without undermining the integrity of the new drug approval process. See pp. __, supra. Advertising of particular compounded drugs, in contrast, is not necessary to the practice of traditional compounding and would permit compounding pharmacists to engage in manufacturing and thus threaten the integrity and safeguarding function of the new drug approval requirements. See pp. __, supra.

The solicitation provisions are also narrowly drawn. Section 353a(a)(2) permits compounding "in limited quantities" before the receipt of a valid prescription for a particular patient if the decision to compound is based on an established relationship among the pharmacist, the practitioner, and the patient. 21 U.S.C. 353a(a)(2) (Supp. V 1999). That provision accords with the traditional practice of compounding, as defined by the National Association of Boards of Pharmacy. See Allen, supra, at xv (compounding is the preparation of a drug "as the result of a practitioner's Prescription Drug Order or initiative based on the pharmacist/patient/prescriber relationship," but "also includes the preparation of drugs * * * in anticipation of Prescription Drug Orders based on routine, regularly observed patterns").

As the court of appeals noted, the FDA interprets Section 353a(a) to permit a pharmacist to "call a physician and recommend a drug compound when a patient comes in with a prescription for a commercial drug and provides information to the pharmacist that indicates that the patient might require a compounded product."

Pet. App. 9a; see also C.A. E.R. 153. That interpretation derives from the language in Section 353a(a) that permits preparation of a compounded drug based on "a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. 353a(a) (Supp. V 1999). The FDA's reasonable interpretation of that language is not, as the court of appeals viewed it (Pet. App. 9a), an exception that undermines the ability of Section 353a to achieve the government's goals. It is instead an example of how Section 353a is narrowly tailored. The pharmacist undertakes the permitted activity in response to the particularized medical needs of an identified patient in the context of an existing practitioner/patient/pharmacist relationship. The activity therefore does not pose a significant danger that the pharmacist is engaging in drug manufacturing, but rather fits squarely within the traditional practice of pharmacy compounding. See pp. __, supra (explaining that traditional compounding customizes medications in response to a patient's special needs and based on a relationship among the pharmacist, the patient, and the prescribing physician).

2. The alternatives suggested by the court of appeals would undermine the government's interests

The court of appeals mistakenly believed that "clear alternatives exist that can advance the government's asserted interest in a manner far less intrusive to the pharmacists' free speech rights." Pet. App. 10a. In fact, the alternatives suggested by the court of appeals -- "disclaimers on compounded drugs explaining that they had not been subject to FDA approval,"

or subjecting all compounded drug products to the FDCA's new drug approval requirements, ibid. -- not only would fail to advance, but would actually undermine, the government's interests.

Reliance on disclaimers is inconsistent with the FDCA's premarket approval process. That regime prohibits the interstate distribution of drugs that the FDA has not found to be safe and effective. Congress has determined that public health and safety are best ensured by requiring manufacturers to establish to the FDA that their drugs are safe and effective for their intended uses before they are distributed widely in commerce. See Hynson, Westcott & Dunning, 412 U.S. at 619, 630; pp. __, supra. That determination is amply supported by Congress's experience over the course of the last century in regulating the manufacture of drugs. See pp. __, supra. Disclaimers would not prevent widespread distribution of drugs that have not been demonstrated to be safe and effective. They thus would not provide a satisfactory alternative for the new drug approval regime that Congress, based on many years of experience, reasonably determined to be necessary to protect the public.

The other alternative suggested by the court of appeals -- subjecting all compounded drugs to the new drug approval process -- would undermine Congress's competing goal of making compounded drugs available in the limited circumstances in which a compounded product is necessary to meet an individual patient's medical needs. As described above, because those circumstances are so limited, and the costs of the premarket approval process are usually so

substantial, requiring compliance with the new drug approval requirements in all cases would effectively eliminate the availability of compounded products to meet individual medical needs. See pp. __, supra.

The court of appeals therefore erred in concluding that Section 353a is not narrowly tailored to achieve the government's substantial interest in balancing the availability of compounding in response to the particular medical needs of individual patients with preventing compounding that is tantamount to manufacturing, which would threaten the integrity of the new drug approval requirements.

CONCLUSION

The judgment of the court of appeals should be reversed, and the case should be remanded with instructions to enter judgment for the petitioners.

Respectfully submitted.

ALEX M. AZAR II
General Counsel
U.S. Department of Health and Human Services

DANIEL E. TROY
Chief Counsel

PATRICIA J. KAEDING
Associate Chief Counsel
U.S. Food & Drug Administration

THEODORE B. OLSON
Solicitor General

ROBERT D. McCALLUM, JR.
Assistant Attorney General

EDWIN S. KNEEDLER
Deputy Solicitor General

MATTHEW D. ROBERTS
Assistant to the Solicitor General

DOUGLAS N. LETTER
KATHERINE S. DAWSON
Attorneys

DECEMBER 2001

Supreme Court, U.S.
FILED
JAN 11 2002
OFFICE OF THE CLERK

No. 01-344

In The

Supreme Court of the United States

TOMMY G. THOMPSON,
Secretary of Health and Human Services, et al.,

Petitioners,

v.

WESTERN STATES MEDICAL CENTER, et al.,

Respondents.

On Writ Of Certiorari
To The United States Court Of Appeals
For The Ninth Circuit

BRIEF OF RESPONDENTS

HOWARD M. HOFFMANN
Counsel of Record
JASON T. LUNDY
DUANE MORRIS LLC
227 W. Monroe St. – Suite 3400
Chicago, Illinois 60606
(312) 499-6700

Attorneys for Respondents

COCKLE LAW BRIEF PRINTING CO., (800) 225-6964
OR CALL COLLECT (402) 342-2831

BEST AVAILABLE COPY

58 pp

QUESTION PRESENTED FOR REVIEW

Whether the advertisement, promotion, and solicitation restrictions contained in the Food and Drug Administration Modernization Act of 1997 violate the First Amendment.

PARTIES TO THE PROCEEDING AND CORPORATE DISCLOSURE STATEMENT PURSUANT TO RULE 29.6

The Respondents are: Western States Medical Center Pharmacy, a Nevada corporation*; Women's International Pharmacy, a Wisconsin corporation; Health Pharmacy, a Wisconsin corporation; College Pharmacy, a Colorado corporation; Wedgewood Village Pharmacy, a New Jersey corporation; ApotheCure, a Texas corporation; and Lakeside Pharmacy, a Tennessee corporation.

None of the Respondents has a parent corporation. None of the Respondents has stockholders that are publicly held companies owning 10% or more of the stock in the corporation.

---

* TKG California Inc. d/b/a Kronos Pharmacy purchased the assets of Western States Medical Center Pharmacy. TKG California Inc. d/b/a Kronos Pharmacy is not a party hereto but has an interest in the proceedings. TKG California Inc. d/b/a Kronos Pharmacy and its parent, The Kronos Group, Inc., and its parent, Exeter Life Sciences, Inc., are not publicly held companies.

TABLE OF CONTENTS

Page

QUESTION PRESENTED FOR REVIEW i

PARTIES TO THE PROCEEDING AND CORPORATE DISCLOSURE STATEMENT PURSUANT TO RULE 29.6 ii

TABLE OF CONTENTS iii

TABLE OF AUTHORITIES vi

STATEMENT OF THE CASE 1

A. Introduction 1

B. Statement of Facts 2

C. 21 U.S.C. Section 353a, State Laws, and the Absence of Restrictions on Compounding 5

SUMMARY OF ARGUMENT 12

ARGUMENT 15

I. THE COURTS BELOW CORRECTLY HELD THAT THE RESTRICTIONS ON TRUTHFUL AND NON-MISLEADING ADVERTISEMENT AND SOLICITATION CONTAINED IN SECTIONS 353a(a) AND (c) VIOLATE THE FIRST AMENDMENT 15

A. Petitioners Have The Burden Of Satisfying The *Central Hudson* Criteria 15

B. Petitioners Have Not Shown That They Have A Substantial Interest 18

C. Petitioners Have Not Shown That The Restrictions On Respondents' Truthful And Non-Misleading Advertising And Soliciting Materially Advance Petitioners' Asserted Interests 23

TABLE OF CONTENTS – Continued

Page

1. FDA's prior enforcement actions are irrelevant to the unconstitutionality of the challenged restrictions but do reveal that the FDA did not consider "compounding" to be "manufacturing" 23

2. The power to regulate compounding, a commercial activity, does not include the power to restrict advertising, promoting and solicitating 25

3. Patient need and physician judgment drive demand for compounds, not advertisement, promotion, and solicitation 28

4. Petitioners have not demonstrated that the challenged speech restrictions will materially prevent a circumvention of the drug approval process 29

5. FDAMA is so riddled with exceptions that it cannot directly and materially advance Petitioners' asserted interest 30

D. Section 353a Does Not Accomplish The Asserted Ends In A Manner That Is No More Extensive Than Necessary 32

II. PHARMACY COMPOUNDED DRUGS ARE NOT NEW DRUGS 34

A. The Inapplicability Of 21 U.S.C. § 321(p)(1) And The Impossibility Of Clinical Trials For Compounds 35

B. The Effects Of 21 U.S.C. §§ 360(a)(1), 360(g)(1), And 374(a)(2)(A) 37

C. Petitioners' Cases Do Not Apply 40

TABLE OF CONTENTS – Continued

Page

D. The FDA's Historical Hands-Off Approach To Pharmacy Compounding 42

E. Adequacy Of Existing Regulations And Patient Protection 44

III. PETITIONERS CANNOT CONDITION EXEMPTION FROM THE FDA'S NEW DRUG APPROVAL PROCESS ON RELINQUISHMENT OF FIRST AMENDMENT RIGHTS 45

CONCLUSION 48

TABLE OF AUTHORITIES

Page

CASES

Bates v. State Bar of Arizona, 433 U.S. 350 (1977) 26

Burson v. Freeman, 504 U.S. 191 (1992) 17, 18

Carey v. Population Serv. Int'l, 431 U.S. 678 (1977) 26

Cedars North Towers Pharmacy, Inc. v. United States, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978) 40

Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n, 447 U.S. 557 (1980) 12, 15, 16, 20, 32

Dolan v. City of Tigard, 512 U.S. 374 (1994) 45, 47

Edenfield v. Fane, 507 U.S. 761 (1993) 16, 17

FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120 (2000) 24, 35, 39

Florida Bar v. Went For It, Inc., 515 U.S. 618 (1995) .. 17, 18

44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484 (1996) ..... *passim*

Greater New Orleans Broad. Ass'n v. United States, 527 U.S. 173 (1999) 26, 29, 30

Ibanez v. Florida Dep't of Bus. & Prof'l Regulation, 512 U.S. 136 (1994) 16, 17, 30

Keyinshan v. Board of Regents, 385 U.S. 589 (1967) 48

Lorillard Tobacco Co. v. Reilly, 121 S. Ct. 2404 (2001) 17, 18, 34, 46

Munro v. Socialist Workers Party, 479 U.S. 189 (1986) 18

TABLE OF AUTHORITIES – Continued

Page

Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999) 24, 27, 28

Pharmanex v. Shalala, 221 F.3d 1151 (10th Cir. 2000) 42

Pickering v. Board of Educ., 391 U.S. 563 (1968) 45, 47

Posadas de Puerto Rico Associates v. Tourism Co. of P.R., 478 U.S. 328 (1986) 46

Professionals & Patients for Customized Care v. Shalala, 56 F.3d 592 (5th Cir. 1995) 24, 41

Professionals & Patients for Customized Care v. Shalala, 847 F. Supp. 1359 (S.D. Tex. 1994) 24

Rubin v. Coors Brewing Co., 514 U.S. 476 (1995) 26, 31, 32, 33

United States v. 9/1 KG. Container, 854 F.2d 173 (7th Cir. 1988) 36, 42

United States v. Ortiz, 422 U.S. 891 (1975) 34, 46

United States v. Rutherford, 442 U.S. 544 (1979) 37, 43

United States v. Sene X Eleemosynary Corp., Inc., 479 F. Supp. 970 (S.D. Fla. 1979), *aff'd*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. 1983) 30, 41

United States v. United Foods, Inc., 121 S. Ct. 2334 (2001) 34, 46

USV Pharm. Corp. v. Weinberger, 412 U.S. 655 (1973) 42

Valley Broad. Co. v. United States, 107 F.3d 1328 (9th Cir. 1997) 26

Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748 (1976) 26, 33

TABLE OF AUTHORITIES – Continued

Page

Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998) 24, 44

Washington Legal Found. v. Friedman, 36 F. Supp. 2d 16 (D.D.C. 1999) 24

Washington Legal Found. v. Henney, 56 F. Supp. 2d 81 (D.D.C. 1999), *vacated at* 202 F.3d 331 (D.C. Cir. 2000) 25

Weinberger v. Bentex Pharm., Inc., 412 U.S. 645 (1973) 29, 37, 39, 42

Weinberger v. Hynson, Wescott & Dunning, Inc., 412 U.S. 609 (1973) 30, 35, 36, 37

Zauderer v. Office of Disciplinary Counsel, 471 U.S. 626 (1985) 16, 17, 30

CONSTITUTION, STATUTES AND REGULATIONS

U.S. Const. Amend. I ..... *passim*

Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq.*

21 U.S.C. § 321(p)(1) (1994) 4, 23, 34, 35, 36, 37

21 U.S.C. § 351(a)(2)(B) (Supp. V 1999) 5, 6

21 U.S.C. § 352(f)(1) (1994 & Supp. V 1999) 5, 6

21 U.S.C. § 353a (Supp. V 1999) ..... *passim*

21 U.S.C. § 353a(a) (Supp. V 1999) ..... *passim*

21 U.S.C. § 353a(a)(1) (Supp. V 1999) 5

21 U.S.C. § 353a(b) (Supp. V 1999) 6

21 U.S.C. § 353a(b)(1)(C) (Supp. V 1999) 6

TABLE OF AUTHORITIES – Continued

Page

21 U.S.C. § 353a(b)(3)(B) (1994 & Supp. V 1999) ..7, 31

21 U.S.C. § 353a(b)(3)(B)(i) (Supp. V 1999) 7

21 U.S.C. § 353a(b)(3)(B)(ii) (Supp. V 1999) 7

21 U.S.C. § 353a(c) (Supp. V 1999) ..... *passim*

21 U.S.C. § 355 (1994 & Supp. V 1999) 5, 6

21 U.S.C. § 360(a)(1) (1994) 8, 13, 37, 38, 40

21 U.S.C. § 360(g)(1) (1994) ..... *passim*

21 U.S.C. § 360(g)(2) (1994) 42

21 U.S.C. § 374(a)(2)(A) (1994) ..... *passim*

Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (21 U.S.C. 353a (Supp. V 1999) ..... *passim*

Wis. Stat. Ann. § 450.01(3) 12, 20

Wis. Stat. Ann. § 450.01(7) 20, 38

Wis. Stat. Ann. § 450.01(13) 20

MISCELLANEOUS

Compliance Policy Guide 7132.16 1

Sen. Rep. No. 105-43 (1997) 3

143 Cong. Rec. S 9811-04 (daily ed. Sept. 24, 1997) ..4, 23

STATEMENT OF THE CASE

A. Introduction

Petitioners' brief raises issues unrelated to the First Amendment and underscores what this case is not about. It is not about dispensing unsafe, ineffective or "unreasonable" quantities of compounded drugs, false or misleading advertisement, or illegal activity. This case is about absolute restrictions on truthful, non-misleading advertisement and solicitation contained in the Food and Drug Administration Modernization Act of 1997 ("FDAMA"), at 21 U.S.C. §§ 353a(a) and (c) (Supp. V 1999), that violate the First Amendment.

This case is before the Court after rulings on cross-motions for summary judgment in the district court and affirmed (in part) by the Ninth Circuit. Petitioners offered no evidence establishing that the distribution of compounded drugs poses a health risk or that Respondents' advertising creates demand for compounds. There is no evidence that Respondents ever practiced pharmacy other than in the regular course and in conformity with federal and State laws. Petitioners' sole "evidence" that the dispensing of compounded prescription drugs caused any alleged health risk was their reference to a double hearsay anecdote in their own Compliance Policy Guide 7132.16 ("CPG"). (Pets.' App. 73a.)[1] Petitioners now attempt to shore-up their barren record with hearsay from websites (Pets.' Br. 27, 34) and journal articles (Pets.'

---

[1] Cites to the appendix attached to Petitioners' petition for *certiorari* are designated "Pets.' App. ___," cites to Petitioners' brief are designated "Pets.' Br. ___."

Br. 28, 35) never presented below, the admissibility of which has never been tested under the rules of evidence.

B. Statement of Facts

Respondents are seven licensed pharmacies, located in seven states, specializing in working with physicians to compound drugs for individual patient needs. Respondents advertise, promote and educate physicians and patients about the availability of particular compounded drugs, classes of drugs, and types of drugs. (Verified Compl., ¶ 27; Grp. Exh. 2 to Verified Compl.)

Compounding is the process whereby a pharmacist, pursuant to a physician's prescription, combines, mixes, or alters ingredients to create a customized medication for a patient for whom a manufactured drug is unavailable. The tripartite relationship under which this occurs, *i.e.*, the interplay between physician, patient and pharmacist, is referred to as the "triad." (Verified Compl., ¶ 29.) This triad is in contrast to manufacturers who have no relationship with either physician or patient, but manufacture for distribution to wholesalers and distributors, do not customize for a patient's unique medical needs, and receive no physician prescriptions. Compounded drugs are prescribed by physicians to address many medical problems including cancer, infertility, PMS, menopause, and pain. Pharmacy compounding is a customary and required part of pharmacy practice, a mandatory subject in most pharmacy schools, and most, if not all, State laws require that pharmacists be proficient in compounding and maintain compounding equipment in their pharmacies. (Verified Compl., ¶¶ 19, 20, 31.)

Pharmacists compound a drug product when: manufactured drugs are unavailable; there is no commercially available product to accomplish a desired medical objective (Verified Compl., ¶ 21(a)); a patient is allergic to a manufactured ingredient (Verified Compl., ¶ 21(b)); a manufactured drug is unavailable in an appropriate dose (Verified Compl., ¶ 21(c)); there is a need for carefully calibrated hormone treatments for infertility, cancer, *etc.* (Verified Compl., ¶ 21(d)); and the patient requires an alternative delivery system, *e.g.*, injection, dermal patch, suppository, *etc.* (Verified Compl., ¶ 21(e).) Compounding pharmacists do not compete with drug manufacturers but provide drugs in the interstitial spaces where a manufactured drug does not exist or is unsuitable.

Because of the specialization among and co-dependence between compounding pharmacists and physicians, it is vital that they establish contact and dialogue. This is accomplished by Respondents' advertisement and solicitation, including presentations at medical conventions. (Verified Compl., ¶¶ 28, 30.) Frequently, but for the pharmacist's consultation, neither physician nor patient would be aware of the availability of dosages, drug delivery systems, or the ability to compound certain particular drugs. (Verified Compl., ¶ 23.) This consultation is a vital component of the pharmacist's role as a professional. (Verified Compl., ¶ 4.)

Compounding is not illegal under State or federal law. "[A]ll States include compounding as a core component of the profession of pharmacy." Sen. Rep. No. 105-43, at 67 (1997). Before FDAMA (and to this day), pharmacy practice and its component, compounding,

have been regulated by State law. By contrast, drug manufacturing has been regulated by federal and State law. *See, e.g.*, 143 Cong. Rec. S 9811-04 at S 9839 (daily ed. Sept. 24, 1997). The Food Drug and Cosmetic Act ("FDCA") specifically exempts pharmacies:

> . . . which maintain establishments in conformance with any applicable local laws regulating the practice of pharmacy . . . which are regularly engaged in dispensing prescription drugs . . . upon prescriptions of practitioners licensed to administer such drugs . . . to patients under the care of such practitioners in the course of their professional practice and which do not, either through a subsidiary or otherwise, manufacture, prepare, propagate, compound or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail.

21 U.S.C. § 374(a)(2)(A) (1994). *See also* 21 U.S.C. § 360(g)(1) (1994). Notwithstanding Petitioners' argument to the contrary, compounds are not mentioned or included in the FDCA's definition of "new drug" at 21 U.S.C. § 321(p)(1) (1994).

Prescriptions for compounded drugs, depending on the Respondent, constitute between 60% and 90% of their total prescription orders. (Verified Compl., ¶ 26; *see also*, Pets.' App. 61a.) The volume of compounded drugs dispensed is determined by physicians evaluating patients' needs. It is not increased by Respondents' advertising beyond pre-existing patient need.

C. 21 U.S.C. Section 353a, State Laws, and the Absence of Restrictions on Compounding

In 1997, Congress enacted § 127 of FDAMA, Pub. L. No. 105-115, 111 Stat. 2296 (21 U.S.C. § 353a (Supp. V 1999)), which amended the FDCA by adding § 503(a), codified at 21 U.S.C. § 353a ("Section 353a"). Section 353a addressed compounded drugs and provided that §§ 351(a)(2)(B), 352(f)(1) and 355[2] of the FDCA shall not apply to a drug product as long as:

- No one compounds a drug product who is not a licensed pharmacist or physician. 21 U.S.C. § 353a(a)(1) (Supp. V 1999).
- No licensed pharmacist or physician dispenses a compounded drug unless it is in response to a prescription order for an individual patient or is based upon a history of such valid prescription orders. 21 U.S.C. § 353a(a) (Supp. V 1999).
- A pharmacist or physician only compounds a drug product from a bulk substance that complies with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, but if such a monograph does not exist, then from a list approved or developed by the Secretary of the United States Department of Health and

---

[2] Section 351(a)(2)(B) established requirements for good manufacturing practices. 21 U.S.C. § 351(a)(2)(B) (Supp. V 1999). Section 352(f)(1) established the requirements for the labeling of approved drugs, including directions for use. 21 U.S.C. § 352(f)(1) (1994 & Supp. V 1999). Section 355 establishes the requirements for approval of new drugs. 21 U.S.C. § 355 (1994 & Supp. V 1999).

Human Services. 21 U.S.C. § 353a(b) (Supp. V 1999).

- No physician or pharmacist compounds a drug that has been withdrawn or removed from the market and which appears on a list published by the Secretary of the United States Department of Health and Human Services. 21 U.S.C. § 353a(b)(1)(C) (Supp. V 1999).[3]

Additionally, §§ 353a(a) and (c) required that Respondents not engage in advertising and soliciting. Section 353a(a) provided in pertinent part:

> Sections 351(a)(2)(B), 352(f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order. . . .

21 U.S.C. § 353a(a). Section 353a(c) provided:

> (c) Advertising and Promotion. A drug may be compounded under subsection (a) of this section only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug, class of drug, or type of drug. The pharmacy, licensed pharmacist, or licensed physician may

[3] Because Respondents believed that these provisions were desirable and severable from the speech restrictions contained in §§ 353a(a) and (c), Respondents argued below that if those speech restrictions were found to be unconstitutional, the court should sever and uphold the non-speech restrictions. The Ninth Circuit rejected Respondents' argument, reversed the district court on this point, and invalidated FDAMA in its entirety. (Pets.' App. 57a-59a.)

> advertise and promote the compounding service provided by the licensed pharmacist or licensed physician.

21 U.S.C. § 353a(c).

Section 353a also provided for a Memorandum of Understanding ("MOU") between the Food and Drug Administration ("FDA") and the States. 21 U.S.C. §§ 353a(b)(3)(B)(i) and (ii) (Supp. V 1999). MOUs were to provide that a compounding pharmacy dispensing interstate is subject to investigation and enforcement by both the State in which the dispensing pharmacy is located and the patient's State. Prior to the enactment of § 353a(b)(3)(B), there were no restrictions on the amount of compounded drugs that a pharmacy could dispense interstate. In response to this lawsuit, Petitioners agreed not to enforce the 5% and companion 19.9% MOU limitations. (Defs. Opp'n to Pls.' Mot. T.R.O., at 9.) Therefore, there has never been a volume limitation under either State or federal law on either interstate or intrastate dispensing of compounded drugs. Even if the percentage limitations had been enforced, realistically there would have been no ban on interstate dispensing of compounds because 20 pharmacies or a chain pharmacy could fill the out-of-state demand, thereby legally nullifying any restriction on interstate dispensing. The only activity restricted by FDAMA was the advertisement, promotion, and solicitation of the compounding of any particular drug, class of drugs, or type of drugs, *i.e.*, speech not conduct.

The fundamental and express differences between manufacturing and compounding are set forth in State pharmacy laws and the FDCA, *i.e.*, 21 U.S.C. §§ 360(a)(1) (1994), 360(g)(1) (1994), and 374(a)(2)(A) (1994). For example, under § 360(a)(1), pharmacy compounding is specifically excluded as it refers to drugs distributed " . . . from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer. . . . " 21 U.S.C. § 360(a)(1). "Distribution" is delivery by a manufacturer to a middleman, while "dispensing" is the act of a pharmacist transferring the drug directly to the patient pursuant to a prescription. Pharmacy compounding results in dispensing. Manufacturing and compounding are not defined in the FDCA, except to the extent that §§ 360(g)(1) and 374(a)(2)(A) provide benchmark characteristics and even then, for definitional purposes, revert back to and rely on State laws.

All States define and regulate the practice of pharmacy within their borders.[4] Twenty-six States

[4] Ala. Code § 34-23-1 *et seq.* (2001); Alaska Stat. § 8.80.003 *et seq.* (Michie 2001); Ariz. Rev. Stat. Ann. § 32-1901 *et seq.* (West 2001); Ark. Code Ann. § 17-92-101 *et seq.* (Michie 2001); Cal [Bus. Prof.] Code § 4000 *et seq.* (Deering 2001); Colo. Rev. Stat. Ann. § 12-22-01 *et seq.* (West 2001); Conn. Gen. Stat. § 20-570 *et seq.* (2001); Del. Code Ann. Tit. 24, § 2501 *et seq.* (2001); D.C. Code Ann. § 48-701 *et seq.* (2001); Fla. Stat. Ch. 465.001 *et seq.* (2001); Ga. Code Ann. § 26-4-1 *et seq.* (Harrison 2001); Haw. Rev. Stat. Ann. § 461-1 *et seq.* (Michie 2001); Idaho Code § 54-1701 *et seq.* (Michie 2000); 225 Ill. Comp. Stat. Ann. 85/1 *et seq.* (West 2001); Ind. Code Ann. § 25-26-13 *et seq.* (Michie 2001); Iowa Code § 155A.1 *et seq.* (2001); Kan. Stat. Ann. § 65-1625 *et seq.* (2001); Ky. Rev. Stat. Ann. § 315.002 *et seq.* (Michie 2001); La. Rev. Stat. Ann. § 1161 *et seq.* (West 2000); Me. Rev. Stat. Ann. Tit. 32 § 13701 *et seq.* (West 2001); Md. Code Ann., [Health Occ.] § 12-101 *et seq.* (2001); Mass. Ann. Laws ch. 94C, § 1 *et seq.* (Law. Co-op. 2001); Mich. Comp. Laws Ann. § 333.17701 *et seq.* (West 2001); Minn. Stat. § 151.01 *et seq.* (2000); Miss. Code Ann. § 73-21-71 *et seq.* (2001); Mo. Rev. Stat. § 338.010 *et seq.* (2001); Mont. Code Ann. § 37-7-101 *et seq.* (2001); Neb. Rev. Stat. Ann. § 71-1,142 *et seq.* (Michie 2001); Nev. Rev. Stat. Ann. 639.001 *et seq.* (Michie 2001); N.H. Rev. Stat. Ann. § 318.1 *et seq.* (2001); N.J. Stat. Ann. § 45:14-1 *et seq.* (West 2001); N.M. Stat. Ann. § 61-11-1 *et seq.* (Michie 2001); N.Y. [Educ.] Law § 6800 *et seq.* (Consol. 2001); N.C. Gen. Stat. § 90-85.2 *et seq.* (2000); N.D. Cent. Code § 43-15-01 *et seq.* (2001); Ohio Rev. Code Ann. § 4729.01 *et seq.* (West 2001); Okla. Stat. tit. 59, § 353-1 *et seq.* (2001); Or. Rev. Stat. § 689.005 *et seq.* (1999); 63 Pa. Stat. Ann. § 390-1 *et seq.* (West 2001); R.I. Gen. Laws § 5-19.1-1 *et seq.* (2001); S.C. Code Ann. § 40-43-10 *et seq.* (Law. Co-op. 2001); S.D. Codified Laws § 36-11-1 *et seq.* (Michie 2001); Tenn. Code Ann. § 63-10-401 *et seq.* (2001); Tex. [Occ.] Code Ann. § 551.001 *et seq.* (Vernon 2001); Utah Code Ann. § 58-17a-101 *et seq.* (2001); Vt. Stat. Ann. tit. 26, § 2021 *et seq.* (2001); Va. Code Ann. § 54.1-3401 *et seq.* (Michie 2001); Wash. Rev. Code Ann. § 18.64.001 *et seq.* (West 2001); W. Va. Code Ann. § 30-5-1 *et seq.* (Michie 2001); Wis. Stat. Ann. § 450.01 *et seq.* (West 2001); Wyo. Stat. Ann. § 33-24-101 *et seq.* (Michie 2001).

also require that out-of-state pharmacies dispensing to patients in their States register in their States and subject themselves to their enforcement.[5] States define

[5] Alaska Stat. § 8.80.158 (Michie 2001); Ark. Code Ann. § 17-92-401 (Michie 2001); Cal [Bus. Prof.] Code § 4112 (Deering 2001); Conn. Gen. Stat. § 20-627 (2001); Del. Code Ann. Tit. 24, § 2538 (2001); Fla. Stat. Ch. 465.0156 (2001); 225 Ill. Comp. Stat. Ann. 85/16a (West 2001); Ind. Code Ann. § 25-26-17-3 (Michie 2001); Iowa Code § 155A.13a (2001); Kan. Stat. Ann. § 65-1657 (2001); Ky. Rev. Stat. Ann. § 315.0351 (Michie 2001); Md. Code Ann., [Health Occ.] § 12-403 (2001); Minn. Stat. § 151.19 (2000); Miss. Code Ann. § 73-21-106 (2001); Mont. Code Ann. § 37-7-703 (2001); Nev. Rev. Stat. Ann. 639.2328 (Michie 2001); N.M. Stat. Ann. § 61-11-14.1 (Michie 2001); N.Y. [Educ.] Law § 6808-b

manufacturing[6] and

(Consol. 2001); N.C. Gen. Stat. § 90-85.21a (2000); N.D. Cent. Code § 43-15-34.1 (2001); Okla. Stat. tit. 63, § 2-302 (2000); R.I. Gen. Laws § 5-19.1-11 (2001); S.D. Codified Laws § 36-11-19.3 (Michie 2001); Va. Code Ann. § 54.1-3434.1 (Michie 2001); Wash. Rev. Code Ann. § 18.64.360 (West 2001); Wyo. Stat. Ann. § 33-24-152 (Michie 2001).

An example is Illinois' statute which provides that, "[t]he Board shall require and provide for an annual nonresident special pharmacy registration for all pharmacies located outside of [Illinois] that dispense medications for Illinois residents and mail, ship, or deliver prescription medications into [Illinois]." 225 Ill. Comp. Stat. Ann. 85/16a(b) (West 2001).

[6] Ala. Code § 34-23-1(11) (2001); Alaska Stat. § 8.80.480(15) (Michie 2001); Ariz. Rev. Stat. Ann. § 32-1901(27) (West 2001); Ark. Code Ann. § 20-64-201(5) (Michie 2001); Cal [Bus. Prof.] Code § 4033 (Deering 2001); Colo. Rev. Stat. Ann. § 12-22-102(17) (West 2001); Conn. Gen. Stat. § 21-240(28) (2001); Del. Code Ann. tit. 24, § 2502 (2001); D.C. Code Ann. § 48-701(3) (2001); Fla. Stat. ch. 499.003(21) (2001); Ga. Code Ann. § 26-4-5(23) (Harrison 2001); Haw. Rev. Stat. Ann. § 328-112 (Michie 2001); Idaho Code § 54-1705(17) (Michie 2000); 225 Ill. Comp. Stat. Ann. 120/15 (West 2001); Ind. Code Ann. § 16-18-2-216 (Michie 2001); Iowa Code § 124.101(16) (2001); Kan. Stat. Ann. § 65-1626(q) (2001); Ky. Rev. Stat. Ann. § 315.010(12) (Michie 2001); La. Rev. Stat. Ann. § 1164(25) (West 2000); Me. Rev. Stat. Ann. tit. 32 § 13702(14) (West 2001); Md. Ann. Code art. 27, § 277 (2001); Mass. Ann. Laws ch. 94C, § 1 (Law. Co-op. 2001); Mich. Comp. Laws Ann. § 333.17706(1) (West 2001); Minn. Stat. § 151.01(Subd. 14) (2000); Miss. Code Ann. § 73-21-73(s) (2001); Mo. Rev. Stat. § 195.010(23) (2001); Mont. Code Ann. § 37-7-101(17) (2001); Neb. Rev. Stat. Ann. § 28-401(14) (Michie 2001); Nev. Rev. Stat. Ann. 639.009 (Michie 2001); N.H. Rev. Stat. Ann. § 318.1(viii) (2001); N.J. Stat. Ann. § 24:6B-12(f) (West 2001); N.M. Stat. Ann. § 61-11-2(Q) (Michie 2001); N.Y. [Educ.] Law § 6802(21) (Consol. 2001); N.C. Gen. Stat. § 90-87(15) (2000); N.D. Cent. Code § 43-15-01(13) (2001); Ohio Rev. Code Ann.

compounding,[7] while neither is defined in the FDCA or FDAMA.

§ 3715.01(14) (West 2001); Okla. Stat. tit. 59, § 351.1(20) (2001); Or. Rev. Stat. § 689.005(19) (1999); 35 Pa. Stat. Ann. § 780-102 (West 2001); R.I. Gen. Laws § 5-19.1-2(n) (2001); S.C. Code Ann. § 40-43-30(29) (Law. Co-op. 2001); S.D. Codified Laws § 34-20B-1(11) (Michie 2001); Tenn. Code Ann. § 63-10-404(18) (2001); Tex. [Occ.] Code Ann. § 551.003(23) (Vernon 2001); Utah Code Ann. § 58-17a-102(22) (2001); Vt. Stat. Ann. tit. 18, § 4201(14) (2001); Va. Code Ann. § 54.1-3401 (Michie 2001); Wash. Rev. Code Ann. § 18.64.011(20) (West 2001); W. Va. Code Ann. § 30-5-1b(o) (Michie 2001); Wis. Stat. Ann. § 450.01(13) (2001); Wyo. Stat. Ann. § 35-7-1002(xiii) (Michie 2001).

[7] Alaska Stat. § 8.80.480(3) (Michie 2001); Ariz. Rev. Stat. Ann. § 32-1901(7) (West 2001); Colo. Rev. Stat. Ann. § 12-22-102(6) (West 2001); Conn. Gen. Stat. § 20-571(5) (2001); Ga. Code Ann. § 26-4-5(4) (Harrison 2001); Haw. Rev. Stat. Ann. § 328-112 (Michie 2001); Idaho Code § 54-1705(17) (Michie 2000); 225 Ill. Comp. Stat. Ann. 85/3(o) (West 2001); Ky. Rev. Stat. Ann. § 315.010(5) (Michie 2001); La. Rev. Stat. Ann. § 1164(5) (2000); Me. Rev. Stat. Ann. tit. 32 § 13702(2-A) (West 2001); Md. Code Ann., [Health Occ.] § 12-101(d) (2001); Miss. Code Ann. § 73-21-73(c) (2001); Mont. Code Ann. § 37-7-101(7) (2001); Neb. Rev. Stat. Ann. § 71-1,142(7) (Michie 2001); Nev. Rev. Stat. Ann. 639.0053 (Michie 2001); N.H. Rev. Stat. Ann. § 318.1(III-a) (2001); N.M. Stat. Ann. § 61-11-2(C) (Michie 2001); N.C. Gen. Stat. § 90-85.3(c) (2000); N.D. Cent. Code § 43-15-01(3) (2001); Ohio Rev. Code Ann. § 4729.01(C) (West 2001); R.I. Gen. Laws § 5-19.1-2(c) (2001); S.C. Code Ann. § 40-43-30(7) (Law. Co-op. 2001); S.D. Codified Laws § 36-11-2(5) (Michie 2001); Tenn. Code Ann. § 63-10-404(4) (2001); Tex. [Occ.] Code Ann. § 551.003(9) (Vernon 2001); Utah Code Ann. § 58-17a-102(6) (2001); Va. Code

SUMMARY OF ARGUMENT

FDAMA's advertisement and solicitation restrictions fail this Court's test for commercial speech restrictions established in *Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n*, 447 U.S. 557 (1980) and, therefore, violate the First Amendment. The parties agree, here and in the courts below, that Respondents' advertisements and solicitations are truthful and non-misleading. In the court below, Petitioners agreed that the introduction of compounds interstate was legal, a position they no longer maintain in this Court.

Petitioners do not have a substantial interest in "preventing manufacturing under the guise of compounding" because Petitioners' purported interest is based on a false premise. The false premise is that pharmacy compounding in compliance with State laws can ever be manufacturing or that they can be differentiated by volume. Petitioners' erroneous position disregards the differences between manufacturing and compounding and falsely attributes advertising and soliciting solely to manufacturing.

In an attempt to achieve that goal, Section 353a restricts truthful, non-misleading speech; however, Respondents' advertising and soliciting do not drive demand for compounded drugs; patients' needs as determined by physicians' prescriptions drive that demand. Advertising informs the physician of the availability of

---

Ann. § 54.1-3401 (Michie 2001); Wash. Rev. Code Ann. § 18.64.011(18) (West 2001); W. Va. Code Ann. § 30-5-1b(c) (Michie 2001); Wis. Stat. Ann. § 450.01(3) (West 2001).

compounded drugs to satisfy a pre-existing patient need. Moreover, the Petitioners, by their own admission, will allow advertising of compounding services, just not of particular compounded drugs, classes of drugs, or types of drugs. Consequently, even were we to assume, *arguendo*, that a restriction prohibiting advertising of services and specific drugs, classes, and types could measurably reduce the demand for compounded drugs, it is doubtful that the FDAMA speech ban on specific drugs, classes, and types could achieve that goal. Further, regardless of the speech restrictions, the many exceptions to FDAMA allow widespread dispensing of compounded drugs such that the advertisement and solicitation restrictions do little to advance Petitioners' asserted interest.

The absolute speech restrictions in §§ 353a(a) and (c) are more extensive than necessary to accomplish Petitioners' purported interest. The Ninth Circuit correctly recognized less intrusive options that would advance Petitioners' interest. For example, disclaimers explaining that compounded drugs did not have FDA approval would accomplish Petitioners' interest without abridging Respondents' First Amendment rights. Petitioners rationalize that compounds are "new drugs" and, therefore, must be put through a new drug approval process.

The FDCA never recognized compounds as new drugs, and the FDA's prior conduct is consistent with this position. Pharmacy compounding is specifically exempted from the FDCA by 21 U.S.C. §§ 360(a)(1), 360(g)(1), and 374(a)(2)(A). It is inconceivable that Petitioners, other than for the purpose of this appeal, genuinely consider interstate dispensing of compounds illegal. As Petitioners admit in their brief, they steadfastly and

historically have refrained from controlling or regulating compounding, and openly acknowledge the desirability of compounding in the niches where manufactured drugs are unavailable. Petitioners assert that "[b]efore 1997, the introduction of compounded new drugs into interstate commerce – like the introduction of all other unapproved new drugs – was unlawful in all circumstances." (Pets.' Br. 18.) They are wrong and ignore the FDA's own complete lack of regulation or enforcement activity towards pharmacies.

The advertisement and solicitation restrictions in Section 353a do nothing more than prevent the dissemination of admittedly truthful, non-misleading information to physicians and patients. Capping the volume of compounds cannot be accomplished by restrictions on advertising or soliciting. Such volume restrictions are provoked by physicians' judgments of patients' needs. The information disseminated is not just advertising, but also educational, *i.e.*, it informs physicians and patients of what is capable of being compounded.

Petitioners cannot condition exemption from FDCA requirements on Respondents' relinquishment of their Constitutional rights because the First Amendment protects Respondents from the Petitioners' attempt to regulate conduct by suppressing speech.

ARGUMENT

I. THE COURTS BELOW CORRECTLY HELD THAT THE RESTRICTIONS ON TRUTHFUL AND NON-MISLEADING ADVERTISEMENT AND SOLICITATION CONTAINED IN SECTIONS 353a(a) AND (c) VIOLATE THE FIRST AMENDMENT

A. Petitioners Have The Burden Of Satisfying The *Central Hudson* Criteria

The parties agree, and the courts below held, that Respondents' advertisements and solicitations constitute commercial speech and that the First Amendment issues in this case are controlled by *Central Hudson* and its progeny. Petitioners also concede that Respondents' advertisements and solicitations are truthful and not misleading.[8] (Pets.' Br. 18.) For the restrictions on advertisement and solicitation in §§ 353a(a) and (c) to pass First Amendment scrutiny, they must satisfy the four *Central Hudson* criteria: (1) the speech at issue must concern lawful activity and not be inaccurate or misleading; (2) the asserted governmental interest must be substantial; (3) the law challenged must directly and materially advance the asserted governmental interest; and (4) the law must accomplish the asserted ends in a manner that is not more extensive than necessary. 447 U.S. at 566. *See also 44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 499-500, 529 (1996).

The parties also agree that "[t]he government has the burden of justifying a commercial speech restriction."

[8] Samples of Respondents' advertisements are in the record. (Grp. Exh. 2 to Verified Compl.)

(Defs.' Mot. Summ. J., at 12.) It has been difficult to pin down Petitioners' position as to whether the introduction of compounds into interstate commerce is legal. In this Court, they say it is "unlawful in all circumstances." (Pets'. Br. 18.) Yet, this is not the position that the district court or the Ninth Circuit understood Petitioners to have taken. The district court found, "[i]n this case, Defendants do not argue that the restrictions at issue involve illegal activity; rather they contend that the targeted speech is misleading." (Pets.' App. 32a; to the same effect, *see*, Defs.' Resp. to Interrogs., ¶ 2.) The Ninth Circuit held, "[o]n appeal, the government does not contend that the prohibited speech is unlawful or misleading." (Pets.' App. 5a.) The parties disagree whether Petitioners have met their burden in showing that the soliciting and advertising restrictions at issue satisfy the second, third and fourth *Central Hudson* criteria.

Central Hudson requires that Petitioners may restrict speech only upon a showing of a substantial interest and that the restriction directly and materially advances the substantial interest in a manner no more extensive than necessary. 447 U.S. at 566. Mere speculation or conjecture by the government in attempting to meet its burden will not suffice. *Edenfield v. Fane*, 507 U.S. 761, 770-71 (1993). "The State's burden is not slight. . . . [It] must demonstrate that the harms it recites are real and that its restrictions will in fact alleviate them to a material degree." *Ibanez v. Florida Dep't of Bus. & Prof'l Regulation*, 512 U.S. 136, 143 (1994). Petitioners cannot satisfy their weighty burden, as they have attempted to here, with arguments that "amount to little more than unsupported assertions." *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 649

(1985); *44 Liquormart, Inc.*, 517 U.S. at 504; *Edenfield*, 507 U.S. at 769.

Petitioners suggest that this Court has *sub silentio* overruled *Edenfield*, *Ibanez* and *Zauderer* and lessened their burden to one based "solely on history, consensus, and 'simple common sense.' " (Pets.' Br. 30.) Petitioners base this claim upon *Lorillard Tobacco Co. v. Reilly*, 121 S. Ct. 2404 (2001). In *Lorillard*, this Court, relying on *Florida Bar v. Went For It, Inc.*, 515 U.S. 618 (1995) stated that, "[w]e have permitted litigants to justify speech restrictions by reference to studies and anecdotes pertaining to different locales altogether, or even, in a case applying strict scrutiny, to justify restrictions based solely on history, consensus, and "simple common sense." 121 S. Ct. at 2422, *quoting Florida Bar v. Went For It, Inc.*, 515 U.S. at 628 (citations and internal quotations omitted). However, in *Florida Bar*, unlike here, significant studies were introduced at trial to support the problem addressed. 515 U.S. at 635. Similarly, in *Lorillard*, this Court's review revealed substantial documentation of the problem of underage use of smokeless tobacco and cigars. 121 S. Ct. at 2408. The record here is void of a basis in common sense, let alone proof, that the speech restrictions directly and materially advance the government's purported interest in lessening compounding activity.

In *Florida Bar*, this Court relied upon *Burson v. Freeman*, 504 U.S. 191 (1992), and upheld the limited prohibition on the solicitation of votes within 100 feet of the entrance to a polling place on election day. *See Burson*, 504 U.S. at 211. In balancing two important constitutional rights, free speech and the right to vote, this Court said

that "because a government has such a compelling interest in securing the right to vote freely and effectively, this Court never has held a State 'to the burden of demonstrating empirically the objective effects on political stability that [are] produced' by the voting regulation in question." *Burson*, 504 U.S. at 208, *citing Munro v. Socialist Workers Party*, 479 U.S. 189, 195 (1986). Neither *Lorillard*, *Florida Bar*, nor *Burson* support Petitioners' contention that "common sense" can substitute for evidence to support Petitioners' claim that the dispensing of compounded drugs significantly increases demand for compounding beyond what it would otherwise be, allegedly endangering health. "Such speculation certainly does not suffice when the State takes aim at accurate commercial information for paternalistic ends." *44 Liquormart, Inc.*, 517 U.S. at 507.

B. Petitioners Have Not Shown That They Have A Substantial Interest

Petitioners claim that the challenged restrictions on truthful speech are justified because they advance Petitioners' interest to a material degree in "preventing compounding that is tantamount to manufacturing" which, if permitted, would threaten to undermine the new drug approval process. (Pets.' Br. 31; *see also* similar claims at Pets.' Br. 13, 14, 28, 33, 34, 35, 40, 43.) Petitioners never define the point at which compounding ends and manufacturing begins, making the assessment impossible due to want of necessary facts and criteria.

Petitioners' argument is premised on an assumption that compounding is capable of being done on a scale

tantamount to manufacturing. (Pets.' Br. 28.) However, regardless of volume, compounding can never be manufacturing and manufacturing can never be compounding. They are not defined in Title 21 of the United States Code, and notwithstanding Petitioners' Interrogatory Answer, "State law is irrelevant to this case" (Defs.' Resp. to Interrog. ¶ 1), these terms are defined under State law. Typically, States define manufacturing as the production of a drug to meet an identified generalized patient need, delivered to distributors and wholesalers who sell to pharmacies which dispense to patients.[9] The manufacturer plays no role in the triad, receives no prescriptions, and does not dispense. In contrast, under State laws, pharmacists compound and dispense.[10] Hence, compounding is incapable of ever being tantamount to manufacturing. Additionally, if and when demand for a compound ever increases to a level where manufacturing becomes practical (*i.e.*, profitable), a manufacturer may bring it to market, whereupon pharmacies will stop making it. Petitioners advocate that a characteristic of manufacturing is volume. No State or federal law supports this *leitmotif*.

The FDCA and FDAMA do not define "compounding" or "manufacturing" and State pharmacy codes do not draw upon volume as a distinguishing characteristic. For example, under the Wisconsin Pharmacy Code, "manufacturing" is defined as the "distribution of the drug . . . from the original place of manufacture to the person

---

[9] *See* footnote 6, *supra*.

[10] *See* footnote 7, *supra*.

who makes final delivery or sale to the ultimate consumer." Wis. Stat. Ann. § 450.01(13). "Manufacturing" contemplates distribution by an individual or entity which is never the patient. "Compound" means to "mix, combine or put together various ingredients or drugs for the purpose of dispensing," Wis. Stat. Ann. § 450.01(3), and "dispense" is defined as "to deliver a prescribed drug . . . to an ultimate user. . . . " Wis. Stat. Ann. § 450.01(7).

Petitioners' unsupported assertion, "that advertising of particular drug products is a business practice that is characteristic of manufacturing, but not of traditional compounding by a pharmacy for an individual need" (Pets.' Br. 33) so that "[e]xpenditures on such advertising therefore are a fair proxy for actual or intended large scale manufacturing" (Pets.' Br. 35) is belied by the pharmacy codes of the 50 states. Even if manufacturers advertise, it does not follow that pharmacies do not or that patients and physicians should be prohibited from receiving truthful information. Blanket bans on commercial speech are disfavored. *See 44 Liquormart, Inc.*, 517 U.S. at 500-502, *quoting Central Hudson*, 447 U.S. at 566, n.9 ("[S]pecial concerns arise from 'regulations that entirely suppress commercial speech in order to pursue a non-speech related policy.' ").

The district court's opinion rejecting Petitioners' argument on this subject is a cogent statement of the fallacy of the government's position:

> The court is not convinced, however, that [Petitioners] have a substantial interest in preventing 'compounding under the guise of manufacturing.' [Petitioners] have offered no definition of

> either manufacturing or compounding, apparently because the Modernization Act itself offers no such definition. Thus, there is no coherent way for this court to determine whether [Petitioners] have a substantial interest in encouraging one while limiting the other. In their argument, [Petitioners] appear to equate high volume distribution with manufacturing and low volume distribution with compounding. In their Motion, they insist that they must "limit the volume of compounding because of the increased health risks associated with a large number of patients receiving drugs that are not subject to the same quality control standards that apply to ordinary manufactured drugs." [Petitioners]' Motion at 21. This framework, however, obviously cannot support [Petitioners]' asserted interest in preventing compounding allegedly done under the guise of manufacturing. First, it does nothing to clarify the difference between manufacturing and compounding. Furthermore, even were the distinction clear, this argument neither explains nor supports the contention that there are "increased health risks associated with a large number of patients" receiving compounded drugs, but that compounded drugs in small quantities produce an overall benefit to the public health.
>
> If, on the other hand, [Petitioners] believe that the relevant distinction is between those drugs that are FDA approved and those that are not, the court agrees that the FDA has a legitimate interest in preventing pharmacists from circumventing FDA requirements by changing the description of their products. To the extent this

is the basis for [Petitioners]' distinction, the court agrees that it is substantial. The problem with this argument is that without more, it ultimately reduces to equating manufacturing with approved drugs and compounding with unapproved drugs. At that point, any interest [Petitioners] assert in making compounded drugs available to individual patients is no long tenable. Therefore, on the facts before it, the court is unable to either identify or acknowledge the significance of the distinction between manufactured and compounded drugs.* For this reason, it cannot agree with [Petitioners] that the Government has a substantial interest in achieving the imprecise and undefined balance it purportedly seeks here.

* * *

(Pets.' App. 42a-44a.)

> In reality, the practical difference in this case between [Petitioners]' notion of manufacturing and compounding may actually be embodied by the precise issue the court must address in this order. Specifically, it appears that [Petitioners] would label pharmacy-initiated drug combining as manufacturing, and patient- or physician-initiated drug combining as compounding. This frames the distinction by looking to whether the pharmacist or other drug producer advertised, promoted or otherwise initiated the sale and use of the particular drug product. Of course, to accept [Petitioners]' distinction, and more importantly, to accept that [Petitioners] have a substantial interest in preserving this distinction, is to agree that [Petitioners] have a substantial interest in preventing

> pharmacists from advertising or promoting particular compounded drugs, because to allow such promotion would be to allow pharmacists to manufacture under the guise of compounding. This conclusion begs the question before the court, which is whether the speech restrictions contained in § 353a are legitimate.

(Pets.' App. 43a, n.9.)

C. Petitioners Have Not Shown That The Restrictions On Respondents' Truthful And Non-Misleading Advertising And Soliciting Materially Advance Petitioners' Asserted Interests

1. FDA's prior enforcement actions are irrelevant to the unconstitutionality of the challenged restrictions but do reveal that the FDA did not consider "compounding" to be "manufacturing"[11]

Petitioners argue that prior to the enactment of FDAMA, the FDA was enforcing the law in a manner consistent with FDAMA and that FDAMA merely brought "the legal status of compounding in line with FDA's longstanding enforcement policy of regulating only drug manufacturing, not ordinary pharmacy compounding." (Pets.' Br. 6, *quoting* 143 Cong. Rec. S 9811-04 at S 9839 (daily ed. Sept, 24, 1997) (Statement of Sen. Kennedy).) Petitioners rely upon the CPG and cases cited at page 36 of their brief to support their claim that before

---

[11] Respondents contest that the FDA has jurisdiction over compounded drugs as they are not "new drugs" under § 321(p)(1), and the FDA's prior non-enforcement is relevant to the analysis of whether compounds are new drugs.

FDAMA, the interstate dispensing of compounds was not permitted. (Pets.' Br. 6, 32-33, 36.) The cases cited by Petitioners at page 36 of their brief are silent on the proposition for which they have been cited and have nothing to do with compounded drugs or truthful and non-misleading advertisements.

Petitioners' reliance on its own enforcement of the FDCA before FDAMA to establish that its enforcement met Constitutional standards is misplaced. First, the CPG itself did not make the advertising or soliciting of compounded drugs illegal. It was a statement of FDA enforcement policy that itself revealed the FDA to have deemed compounding not illegal manufacturing when conducted in conformance with the nine CPG factors. Second, the CPG was not law. It was merely an unenforceable internal guide for FDA field agents. *See Professionals & Patients for Customized Care v. Shalala*, 847 F. Supp. 1359, 1363-64 (S.D. Tex. 1994), *aff'd* at 56 F.3d 592 (5th Cir. 1995) ("*PPCC*"). As the court in *PPCC* held, "a policy statement announces the agency's tentative intentions for the future." 56 F.3d at 596.

Courts have not hesitated to declare illegal the enforcement policies of the FDA based on internal guidelines. *See, e.g., FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (invalidating FDA's regulations over tobacco); *Pearson v. Shalala*, 164 F.3d 650, 661 (D.C. Cir. 1999) (invalidating on First Amendment grounds FDA regulation regarding diet supplements); *Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 74 (D.D.C. 1998) (invalidating on First Amendment grounds policies of FDA and HHS restricting off-label uses of FDA-approved drugs and devices); *Washington Legal Found. v.*

Friedman, 36 F. Supp. 2d 16 (D.D.C. 1999); *Washington Legal Found. v. Henney*, 56 F. Supp. 2d 81, 87 (D.D.C. 1999) (finding FDA's policies restricting the dissemination of articles and texts relating to off-label use in violation of the First Amendment, *vacated at* 202 F.3d 331 (D.C. Cir. 2000) because FDA conceded on appeal that it had no authority to prosecute manufacturers for violating a normative standard set forth in FDAMA or the guidelines for continuing medical education).

2. The power to regulate compounding, a commercial activity, does not include the power to restrict advertising, promoting, and soliciting

If compounded drugs filled in response to a physician's prescription are dangerous, then compounding should be outlawed. Yet, State pharmacy codes and pharmacy schools mandate compounding equipment and skills, compounding is specifically exempted by federal statutes, the FDA left compounding alone for at least 59 years, and Petitioners praise compounding, conceding its importance and necessity. Nonetheless, Petitioners struggle to withhold truthful, non-misleading information about an acclaimed and legal activity.

This Court has made it clear that the government may not employ restrictions on accurate commercial speech about lawful activity to regulate the underlying activity which the government seeks to affect. As this Court stated in *44 Liquormart*:

> . . . we think it quite clear that banning speech may sometimes prove far more intrusive than

> banning conduct. . . . In short, we reject the assumption that words are necessarily less vital to freedom than actions, or that logic somehow proves that the power to prohibit an activity is necessarily "greater" than the power to suppress speech about it.

517 U.S. at 511. *See also Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 773 (1976) (holding that a State may not "completely suppress the dissemination of concededly truthful information about entirely lawful activity, fearful of that information's effect upon its disseminators and its recipients.").

Petitioners argue that the advertising and soliciting restrictions advance a substantial governmental interest in that reducing advertising will reduce demand, thereby protecting the public health from compounded drugs. (Pets.' Br. 35.) This Court has consistently rejected this rationale as a justification for limitations upon advertising. *See, e.g., 44 Liquormart, Inc.*, 517 U.S. at 500, n.10 (striking down two Rhode Island statutes that prohibited the advertising of alcoholic beverage retail prices anywhere other than at point of purchase); *Rubin v. Coors Brewing Co.*, 514 U.S. 476, 491 (1995) (invalidating federal statute that prohibited brewers from disclosing on labels the alcoholic content of their beers); *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 772 (1975) (declaring unconstitutional a Virginia statute that made it unprofessional for a pharmacist to advertise the prices of prescription drugs). *See also Valley Broad. Co. v. United States*, 107 F.3d 1328 (9th Cir. 1997); *Carey v. Population Serv. Int'l.*, 431 U.S. 678 (1977); *Bates v. State Bar of Arizona*, 433 U.S. 350 (1977); *but cf., Greater*

New Orleans Broad. Ass'n v. United States, 527 U.S. 173, 188-89 (1999) (holding unconstitutional statute and regulations that prohibited radio and television broadcasters from carrying advertisements about privately operated commercial casino gambling but recognizing government's interest in alleviating casino gambling's social costs by limiting demand).

The assertion that speech restrictions advance the public health has been rejected by the D.C. Circuit in *Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999). In *Pearson*, the FDA argued that the health of consumers was directly advanced by barring health claims about dietary supplements not approved by the FDA. *Pearson*, 164 F.3d at 656. Here, in a rehash of their position rejected in *Pearson*, Petitioners argue that the health of consumers is advanced by barring all advertisements of compounded drugs because they have not been approved by the FDA. In rejecting the FDA's argument in *Pearson*, the D.C. Circuit wrote:

> The government simply asserts its 'common sense judgment' that the health of consumers is advanced *directly* by barring any health claims not approved by the FDA. Because it is not claimed that the product is harmful, the government's underlying – if unarticulated – premise must be that consumers have a limited amount of either attention or dollars that could be devoted to pursuing health through nutrition, and therefore products that are not indisputably health enhancing should be discouraged as threatening to crowd out more worthy expenditures. We are rather dubious that this simplistic view of human nature or market behavior is sound, but, in any event, it surely cannot be said

> that this notion – which the government does not even dare openly to set forth – is a *direct* pursuit of consumer health; it would seem a rather indirect route, to say the least.

164 F.3d at 656.

3. Patient need and physician judgment drive demand for compounds, not advertisement, promotion, and solicitation

No matter how widely Respondents truthfully advertise particular drugs, classes and types of drugs, patients cannot obtain a compounded drug without a valid prescription from a licensed physician. To the extent advertising drives demand for compounds, the judgment of the prescribing physician serves as a brake. Unlike consumer products for which demand can be artfully hyped, advertising compounded drugs merely informs physicians and patients about the availability of compounds, but only to meet a pre-existing medical need. In the triad, the pharmacist is not a pitchman, but a learned professional. The pharmacist educates the physician of treatment opportunities which the physician may then prescribe but only upon diagnosis of a patient with that particular need.

Petitioners offered no evidence that Section 353a's advertisement and solicitation restrictions would directly and materially further the government's goal to reduce demands for compounds. As this Court observed when considering gambling advertising, "[w]hile it is no doubt fair to assume that more advertising would have some

impact on overall demand for gambling, it is also reasonable to assume that much of that advertising would merely channel gamblers to one casino, rather than another." *Greater New Orleans Broad. Ass'n v. United States*, 527 U.S. 173, 189 (1999). The speech restrictions in Section 353a do not directly and materially advance the government's purported interest.

4. Petitioners have not demonstrated that the challenged speech restrictions will materially prevent a circumvention of the drug approval process

Petitioners claim that the speech and advertising restrictions contained in §§ 353a(a) and (c) will prevent circumventing the new drug approval process. Petitioners rely upon *Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645, 653 (1973), in which this Court noted "that it would be 'inherently unfair' to require compliance by one manufacturer with the new drug approval requirements 'while his competitors marketing similar drugs remain free to violate the Act.' " (Pets.' Br. 29.) Manufacturers and pharmacists do not compete, and Petitioners offered no evidence of this mythical competition. By definition, pharmacies only compound in the absence of a suitable manufactured product. (Verified Compl., ¶ 21(a).) It ill behooves Petitioners to complain that compounds bypass the new drug approval process. Compounds were never subject to the new drug approval process, which would not have changed under FDAMA. The only change would have been the imposition of First Amendment restrictions which would not have directly and materially protected the new drug approval process.

Petitioners claim that the advertisement and solicitation restrictions protect the public because public health risk increases when more patients use compounded drugs.[12] (Pets.' Br. 30.) In the lower courts, Petitioners based this claim on one anecdotal incident reported as hearsay in the CPG. In this Court, Petitioners again rely upon this isolated anecdotal incident. (Pets.' Br. 28.) As the court recognized in *United States v. Sene X Eleemosynary Corp., Inc.*, 479 F. Supp. 970, 976 (S.D. Fla. 1979), *aff'd*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. 1983), such "anecdotal evidence . . . is the poorest form of evidence." In *Weinberger v. Hynson, Westcott & Dunning, Inc.*, this Court characterized anecdotal evidence as "treacherous." 412 U.S. 609, 629-630 (1973). Speculative conjecture will not satisfy Petitioners' burden in justifying the speech and advertising restrictions at issue. *Ibanez v. Florida Dep't of Bus. & Prof'l Regulation*, 512 U.S. 136, 141-142 (1994); *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 647 (1985).

5. FDAMA is so riddled with exceptions that it cannot directly and materially advance Petitioners' asserted interest

When a statutory or regulatory scheme is "so pierced by exemptions and inconsistencies, [ ] the Government cannot hope to exonerate it." *Greater New Orleans Broad. Ass'n*, 527 U.S. at 190. Petitioners' aim is to suppress the

---

[12] The cases relied upon by Petitioners at footnote 4 of their brief are irrelevant here. They had nothing to do with compounding by a licensed pharmacist, and none were First Amendment cases.

volume of compounded drugs. Yet, regardless of the speech restrictions, FDAMA permits widespread compounding.

FDAMA permitted pharmacies to dispense unlimited quantities of prescription drugs intrastate. Moreover, nothing made it illegal for patients to cross state lines and purchase compounds in a neighboring state, and FDAMA did not prevent a physician from prescribing a compound in any quantity or frequency.

The MOU provisions did nothing to stem interstate dispensing. Pursuant to § 353a(b)(3)(B), if a compounding pharmacist's State did not enter into an MOU, a pharmacist could dispense compounds interstate up to 5% of total prescription orders. With an MOU, the pharmacist would be permitted to dispense compounds interstate up to 19.9% of total prescription orders.

With their numerous sites, chain drug stores (Walgreens, CVS, *etc.*) could single-handedly endrun the percentages and supply 100% of the demand. Also, to avoid the 5% or 19.9% limitations, pharmacies could merely refer prescriptions over their limit to another pharmacy. That pharmacies can dispense compounds without limits but cannot advertise or solicit their compounds indicates the irrationality of FDAMA's regulatory scheme. *See Rubin v. Coors Brewing Co.*, 514 U.S. 476, 488 ("The failure to prohibit the disclosure of alcohol content in advertising, which would seem to constitute a more influential weapon in any strength war than labels, makes no rational sense if the Government's true aim is to suppress strength wars.").

FDAMA was ill-conceived because the 5% and 19.9% represent a percentage of each pharmacy's total prescription orders. Pharmacies that compound as a specialty and have few sales other than compounds would never have a gross order figure from which to make the calculation, because they would not be able to make a sale of a compound without first making sales of non-compounded drugs.

D. Section 353a Does Not Accomplish The Asserted Ends In A Manner That Is No More Extensive Than Necessary

The Ninth Circuit correctly found that "the speech restrictions fail the fourth *Central Hudson* factor; they are more extensive than necessary to achieve the asserted government interest." (Pets.' App. 10a.) In the district court, Petitioners argued that the speech restrictions were necessary to protect the public from being misled into believing that they were taking prescription drugs that had been approved by the FDA. (Defs.' Mot. Summ. J. at 16-17.) This argument has since been abandoned. The district court and the Ninth Circuit recognized that disclaimers could accompany compounded drugs, explaining that they had not been FDA approved. The availability of options which could advance Petitioners' asserted interests in a manner less intrusive of Respondents' First Amendment rights indicates that the speech restrictions are more extensive than necessary. *See Rubin v. Coors Brewing Co.*, 514 U.S. at 491.

Petitioners now complain that disclaimers would not prevent "widespread distribution of drugs that have not

been demonstrated to be safe and effective." (Pets.' Br. 45.) The disclaimer was in response to Petitioners' lower court argument that compounds are inherently misleading, *i.e.*, that they somehow suggest FDA approval. The speech restrictions are far broader than necessary, while at the same time do little, if anything, to limit compounded drugs.

Petitioners argue that the challenged restrictions on truthful speech are limited intrusions upon advertising and soliciting because the statute permits Respondents to advertise "that they perform compounding services, that they are experts in compounding, and that they stand ready to fill prescriptions for compounded drug products." (Pets.' Br. 43.) The restrictions on truthful advertising and soliciting contained in § 353a(c) are absolute restrictions upon truthful speech. Section 353a(c) provides that Respondents may not "advertise or promote the compounding of any particular drug, class of drug or type of drug." 21 U.S.C. § 353a(c). It restricts all advertising and soliciting on those topics, whether made in the pharmacy, at seminars, *etc.* Those restrictions prevent the very types of advertisement and promotion that this Court held could not be restricted in other cases. *See, e.g., 44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484 (1996); *Rubin v. Coors Brewing Co.*, 514 U.S. 476 (1995); *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976).

II. PHARMACY COMPOUNDED DRUGS ARE NOT NEW DRUGS

Although Petitioners did not so argue in the Ninth Circuit, they now argue that the introduction of compounds into interstate commerce is "unlawful in all circumstances." (Pets.' Br. 18.) Whether pharmacy compounded drugs are "new drugs" and, hence, illegal to introduce into interstate commerce is the easiest issue for this Court because Petitioners represented in the Ninth Circuit that they "do not contend on appeal that the speech prohibited by section 353a concerns illegal activity or is misleading." (*See* Brief for Appellants in the Ninth Circuit Court of Appeal, at 27, n.10.) This issue has no place in this Court, as it was given token lip service in the district court, was unsupported by law and evidence, and expressly waived in the Ninth Circuit. Petitioners should be held to that waiver, as they prevented the lower court from deciding that issue. *See Lorillard Tobacco Co. v. Reilly*, 121 S. Ct. 2404, 2419 (2001) ("[W]e decline to reach an issue that was not decided below"); *United States v. United Foods, Inc.*, 121 S. Ct. 2334, 2340 (2001) (declining to reach argument not raised or addressed in the Court of Appeals and rejecting claim that argument was embraced within the question set forth in the petition for *certiorari*); *United States v. Ortiz*, 422 U.S. 891, 896 (1975).

Petitioners' original position was that Respondents' speech was inherently untruthful and misleading. (*See* Defs.' Resp. Interrog., ¶ 2.) Petitioners shifted their argument and now contend that compounds are "new drugs" pursuant to 21 U.S.C. § 321(p)(1) and, therefore, illegal to

introduce into interstate commerce without having satisfied the FDA's new drug approval process. Alas, compounding was never illegal under the FDCA and was not treated as illegal by the FDA before the CPG or in the CPG.

Petitioners' jurisdiction to address compounds as new drugs, if existent at all, would have to derive from the "new drug" definition in 21 U.S.C. § 321(p)(1). This is the foundation from which Petitioners maintain they can extract the surrender of First Amendment rights. To confer upon the FDA jurisdiction over compounds as "new drugs," there would have to be an explicit statutory grant of authority. *See, e.g., FDA v. Brown & Williamson*, 529 U.S. 120 (2000).

A. The Inapplicability Of 21 U.S.C. § 321(p)(1) And The Impossibility Of Clinical Trials For Compounds

Compounds are drugs, but not "new drugs." The determination of what is a new drug starts with an analysis of 21 U.S.C. § 321(p)(1), which requires expert evaluation for safety and effectiveness – an evaluation Petitioners represent requires in excess of $200 million. (Pets.' Br. 26.) Petitioners point out that this would be "uneconomical." (Pets.' Br. 27.) It would not only be uneconomical but impossible. To satisfy the clinical trial component of the approval process requires not only untold millions of dollars, but a statistically valid sample. *Weinberger v. Hynson, Wescott & Dunning, Inc.*, 412 U.S. 609 (1973), demonstrates the impossibility of applying § 321(p)(1) to compounds because of the need to present

"substantial evidence of effectiveness" for a new drug, which this Court held included "evidence consisting of adequate and well controlled investigations, including clinical investigations." *Hynson*, 412 U.S. at 614, 617. *See also United States v. 9/1 KG. Container*, 854 F.2d 173, 177 (7th Cir. 1988) (discussing veterinary drugs, the court held that a new drug " . . . requires data from large populations of animals and the application of *powerful statistical techniques.*") (emphasis added). The unavoidable dilemma, revealing these provisions incapable of application to compounded drugs, is that compounded drugs are patient-specific, typically varying in dose levels, composition, and even delivery form from patient to patient.

Petitioners' references to § 321(p)(1) always omit critical, operative words and phrases. Petitioners always only recite the "not generally recognized [ ] among experts" portion, while always omitting the "to evaluate the safety and effectiveness" portion. A key element of § 321(p)(1) is evaluation, and as Petitioners themselves report, this takes not just vast sums of money, but a vast patient database. (Pets.' Br. 26-27.) This database will never exist for compounds. Section 321(p)(1) requires that, to qualify as a new drug, the expert recognition comes after intense evaluation and, hence, must be capable of being evaluated. This "evaluation" is impossible for compounds because compounds fill extemporaneous needs not met by manufactured drugs and, consequently, would never generate a sufficiently sizeable statistical base upon which to determine safety and efficacy to the degree required for a new drug. This standard has never

been applied to compounds and, if it ever were, compounds would be eliminated, other than on a purely intrastate basis.

Petitioners' own cases establish that the new drug approval requirements cannot be applied to compounds. *See, e.g., Hynson*, 412 U.S. at 618 (a test drug must be "standardized as to identity, strength, quality, purity and dosage form to give significance to the results of the investigation") (citation omitted); *United States v. Rutherford*, 442 U.S. 544, 553 (1979) (effectiveness of new drug must be "formed on substantial evidence"); *Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645, 652 (1973) (whether a drug is a new drug " . . . depends in part on expert knowledge and experience . . . based on controlled clinical experimentation and backed by substantial support"). These cases establish that compounds are categorically incapable of being subjected to the intense investigation required of new drugs. Compounds are not standardized, as required by *Hynson* and, by definition, do not exist in sufficient quantities for clinical trials.

B. The Effects Of 21 U.S.C. §§ 360(a)(1), 360(g)(1), And 374(a)(2)(A)

Section 321(p)(1) does not mention compounds, while other sections of Title 21 of the United States Code overwhelming support the proposition that pharmacy compounding, if compliant with these sections, is not covered by the FDCA. *See* 21 U.S.C. §§ 360(a)(1), 360(g)(1), and 374(a)(2)(A). Petitioners acknowledge that § 321(p)(1) applies only to manufacturers and distributors. Manufacturers and distributors must obtain approval, *i.e.*,

undergo the referenced evaluation, must satisfy the FDA that the drug is safe and effective, and must register, report, and be inspected by the FDA. (Pets.' Br. 2-3.)

There is no federal definition of manufacturing or compounding. (*See*, Pets.' App. 42a.) Their definitions are left exclusively to the States,[13] which definitions do not take into account volume or interstate activity. This reliance on State enforcement and adoption of State definitions is expressly incorporated into §§ 360(a)(1), 360(g)(1), and 374(a)(2)(A). Against this backdrop we address §§ 360(a)(1), 360(g)(1), and 374(a)(2)(A). Section 360(a)(1) expressly provides that the registration requirement only applies to persons or entities who distribute "from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user." 21 U.S.C. § 360(a)(1).[14] This, without more, completely excludes pharmacies, because it is they which dispense to the ultimate consumer or user under State laws and § 360(a)(1).

The complete exclusion from registration found in §§ 360(a)(1) and (g)(1) is critical, as it immunizes pharmacies from the FDCA's jurisdiction if they dispense to

---

[13] *See* footnotes 6 and 7, *supra*.

[14] Compare the language of § 360(a)(1), "from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user" to the language in Wis. Stat. Ann. § 450.01(7), " 'Dispense' means to deliver a prescribed drug . . . to an ultimate user . . . by or pursuant to the prescription order of a practitioner, including the compounding . . . necessary to prepare the prescribed drug . . . for delivery."

the ultimate consumer, pursuant to a physician's prescription, in conformity with State laws. Any entity that does not need to register is beyond the FDA's reach. In *FDA v. Brown & Williamson Tobacco, Corp.*, 529 U.S. 120 (2000), this Court held that, "[a] court must therefore interpret the statute as a symmetrical and coherent regulatory scheme, and fit, if possible, all parts into a harmonious whole." 529 U.S. at 133 (internal citations and quotations omitted). There is no statutory grant in the FDCA that gives the FDA jurisdiction over compounded drugs as new drugs. As this Court found in *Brown & Williamson*,

> . . . an administrative agency's power to regulate in the public interest must always be grounded in a valid grant of authority from Congress. And in our anxiety to effectuate the congressional purpose of protecting the public, we must take care not to extend the scope of the statute beyond the point where Congress indicated it would stop.

Id. at 151 (internal citations and quotations omitted). *See also Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645, 652 (1973) ("[p]arties, of course, cannot confer jurisdiction; only Congress can do so").

Here, not only is there no such grant, but the FDCA explicitly excludes compounding pharmacies from registration and inspection. Once excluded from registration, compounding cannot be manufacturing since manufacturers must register. If compounds were new drugs, then the FDA would be entitled to demand registration so as to inspect the plant where the new drug is manufactured. The identical, unequivocal provisions of §§ 360(g)(1) and

374(a)(2)(A) further isolate pharmacies from the FDCA, as long as they comply with these sections.

C. Petitioners' Cases Do Not Apply

Petitioners rely on cases which do not support the proposition that pharmacy compounding in compliance with State laws is either manufacturing or creates new drugs. In *Cedars North Towers Pharmacy, Inc. v. United States*, [1978-79 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978), Cedars was accused of packaging and shipping medications to physicians, thereby presumably taking it out of the §§ 360(a)(1), 360(g)(1), and 374(a)(2)(A) exemptions. The court in *Cedars* set out factors which, in the context of the case, it considered to be relevant in determining whether Cedars was exempt under § 360(g)(1). Not one factor related to a First Amendment restriction. Moreover, Cedars advertised products at wholesale prices, hence, not "at retail" as required by Sections 360(g)(1) and 374(a)(2)(A); and its products were also shipped exclusively to physicians for resale and not to the ultimate user. *Cedars* determined that a pharmacy is entitled to an exemption and that it needed to determine whether Cedars had "come dangerously close to crossing the line separating a pharmacy . . . from a manufacturer of drugs. . . . " *Cedars* determined that "the facts compel the conclusion that Cedars had so clearly transcended the level of normal pharmacy operation as to leave no question. . . . " *Cedars* specifically held that "the uncontested facts contained in the record required the conclusion that Cedars is compounding and selling drugs other than the

regular course of the pharmacy dispensing and selling drugs at retail."

In *Professionals & Patients for Customized Care v. Shalala*, 56 F.3d 592 (5th Cir. 1995) ("*PPCC*"), the court held that "[p]harmacies that practice traditional compounding are regulated primarily by state law and the drugs that they blend are exempt from many federal misbranding provisions." 56 F.3d at 593. *PPCC* recognized that pharmacies may not compound and sell to third parties for resale to patients without running the risk of losing their status as an excluded retail entity. *Id.* at 594. *PPCC* did not find that compounds are new drugs, but did find that the FDA's CPG was not a substantive rule. *Id.* Because it was not a substantive rule, the CPG did not impose any rights and obligations on pharmacies. *Id.* at 595. Notwithstanding Petitioners' self-serving reliance on the CPG as a historical marker, to the extent *PPCC* has any relevance, it is in the finding " . . . that traditional compounding activity is not the subject of this CPG 7132.16." *Id.* at 602.

In *United States v. Sene X Eleemosynary Corp., Inc.*, 479 F. Supp. 970 (S.D. Fla. 1979), a manufacturer was trying to parade as a pharmacy. While Sene X was compounding after the receipt of a "prescription," it was filled by one pharmacy that compounded one product. *Sene X*, 479 F. Supp. at 979. It was not extemporaneous compounding because the physician did not have any influence as to the ingredients, dosage, or delivery form. *Id.* at 978-79. In *Sene X*, the court noted that it did not address the issue whether the customary practice of pharmacy is an exemption from the new drug provisions. *Id.* at 978.

Pharmanex v. Shalala, 221 F.3d 1151 (10th Cir. 2000) dealt with manufacturers, and the FDCA's pharmacy exemption provisions were not an issue. It is clear the case related to a manufacturer which made no pretense otherwise. *Pharmanex*, 221 F.3d at 1153. In *Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645 (1973), the defendant was not a pharmacy but a "drug marketer." 412 U.S. at 647. There is no mention of any pharmacy exemptions, and it would be a fair read that it involved exclusively marketers who either were or represented manufacturer(s). Similarly, *USV Pharm. Corp. v. Weinberger*, 412 U.S. 655 (1973), was brought by a "drug marketer" but the Court did not reveal whether the marketer was a manufacturer or distributor for a manufacturer. However, since there was no discussion of pharmacy compounding and a New Drug Application had issued, it could not have been a pharmacy compounding case. *Id.* at 664. In *United States v. 9/1 KG. Containers*, 854 F.2d 173 (7th Cir. 1988), the court held that § 360(g)(2) applies to all drugs made from components that may be lawfully obtained and compounded. 854 F.2d at 179. Therefore, compounding with lawfully obtained ingredients is not prohibited conduct.

D. The FDA's Historical Hands-Off Approach To Pharmacy Compounding

Petitioners have never been able to explain or reconcile how they seek to preserve the availability of compounded drugs (Pets.' Br. 19), while at the same time maintaining that before FDAMA, "the introduction of all other unapproved new drugs – was unlawful in all circumstances" (Pets.' Br. 18) or explain how restricting First Amendment rights aids this reconciliation. Petitioners

argue that their historical 59-year inaction towards pharmacy compounding is the result of a deliberate benign forbearance. A more reasoned explanation for Petitioners' 59-year inaction is their recognition that compounding, compliant with the previously cited sections, was outside its jurisdiction.

In *Rutherford*, this Court held that the FDA's implementation scheme was a salient factor in considering what the FDCA was intended to cover, and relied on the fact that the FDA had never made an exception for drugs for the terminally ill. 442 U.S. at 553. Likewise, the FDA has an uninterrupted 59 plus year history of not requiring compounds to be subjected to the new drug approval process. It is as valuable to consider the FDA's implementation history by omission as commission.

If this long-standing non-intervention was the consequence of benevolent tolerance, then the FDA is admitting that for generations it knowingly permitted illegal activity. This 59-year period is itself expert evidence that compounds are not new drugs. Petitioners admit the "FDA's longstanding enforcement policy of regulating only drug manufacturing, not ordinary pharmacy compounding." (Pets.' Br. 6.) They further concede that the FDA only took action when compounding was outside the scope of normal pharmacy practice, meaning that if compounding was within the scope of normal pharmacy practice, the FDA did not take action because it was not illegal under the FDCA, and the FDA had no jurisdiction.

Interference with the availability and sources for compounds compromises the physicians' prerogative to prescribe and treat. Compounding is a physician driven

therapy. Petitioners permit physicians to prescribe commercially available drugs for off label uses. Prescribing a compound is akin to a physician prescribing off label uses. *See Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d 51, 55 (D.D.C. 1998) ("A physician may prescribe an approved drug for any medical condition, irrespective of whether FDA has determined that the drug is safe and effective with respect to that illness.").

E. Adequacy Of Existing Regulations And Patient Protection

The absence of FDAMA does not create unreasonable risks. If risk was a legitimate concern, then, as Judge Ezra pointed out in his Opinion, the FDA could entirely prohibit compounding. (Pets.' App. 34a.) Further, if safety and efficacy were indeed meaningful concerns, then First Amendment restrictions are meaningless, as they afford no protection.

The patient's protections include the physician's diagnosis and determination of appropriate therapy, issuance of a prescription, evaluation of that prescription, which includes application of her training and judgment as a licensed professional, and collaboration between them. In addition, the pharmacy codes and enforcement activities of all the States in which the pharmacies are located, and 26 States into which they dispense, provide added protection. It is further telling that notwithstanding their penchant for anecdotal "evidence," Petitioners offer no modern examples of problems with compounds. Petitioners also never reference the FDA approved drugs which proved unsafe after entering the market.

It is conceivable that some time, some pharmacy will operate outside the exclusions set up in the FDCA and beyond the scope of State laws. On that day, the FDA and State authorities will be able to take enforcement action against that pharmacy which took itself outside the exemptions. However, this enforcement goal and scheme is not advanced by the First Amendment restrictions.

It is irreconcilable for Petitioners to maintain that the interstate dispensing of compounds is illegal under all circumstances after Petitioners and Congress have routinely, historically, and consistently permitted, tolerated, praised, protected and endorsed compounding in statutes and in all briefs in this case.

III. PETITIONERS CANNOT CONDITION EXEMPTION FROM THE FDA'S NEW DRUG APPROVAL PROCESS ON RELINQUISHMENT OF FIRST AMENDMENT RIGHTS

Respondents maintain compounds are not new drugs. In the event this Court disagrees with that contention, Respondents further maintain an exemption cannot be conditioned on restrictions of First Amendment rights. Petitioners assert that FDAMA's exemption of compounds from the FDCA's new drug approval requirements is contingent upon pharmacies' surrender of their First Amendment right to advertise and solicit. (Pets.' Br. 7-8, 18-19, 42-43.) Petitioners claim that the "government may condition a benefit on their relinquishment of a constitutional right if waiver of the right is reasonably related to the benefit." (Pets.' Br. 42-43, *citing Dolan v. City of Tigard*, 512 U.S. 374, 385, 391 (1994) and *Pickering v.*

Board of Educ., 391 U.S. 563, 568 (1968).) Petitioners did not raise this argument anywhere below and, hence, this Court should not reach that issue. *See, e.g., Lorillard Tobacco Co. v. Reilly*, 121 S. Ct. 2404, 2420 (2001) ("We decline to reach an issue that was not decided below."); *United States v. United Foods, Inc.*, 121 S. Ct. 2334, 2340 (2001); *United States v. Ortiz*, 422 U.S. 891, 896 (1975).

The claim is based on false assumption as well as a syllogism previously rejected by this Court. Petitioners' purported "exemption" of compounds is illusory. As discussed above (Part II, *supra*), by statute and FDA conduct, compounds are not and have never been treated as "new drugs." Petitioners have attempted to create a hollow bargain – that Respondents must forego their First Amendment rights to advertise and solicit in exchange for an exemption from regulation that is inapplicable in the first place. To dispense compounds, Respondents need not relinquish their First Amendment rights.

If, hypothetically, the Court were to find that compounds are new drugs, Petitioners nonetheless cannot condition an exemption upon Respondents' relinquishment of First Amendment rights. *See 44 Liquormart Inc. v. Rhode Island*, 517 U.S. 484, 513 (1996) (Stevens, J., joined by Kennedy, J., Thomas, J., and Ginsburg, J.) ("it does not follow that conferral of the benefit may be conditioned on the surrender of a constitutional right"). Although the Court tolerated such a scheme in *Posadas de Puerto Rico Associates v. Tourism Co. of P.R.*, 478 U.S. 328 (1986), the Court has since rejected Petitioners' position as a false syllogism. *See 44 Liquormart*, 517 U.S. at 510-14. *44 Liquormart* distinguished and disavowed that "greater-includes-the-lesser" argument because "it is inconsistent with both

logic and well-settled doctrine." *44 Liquormart*, 517 U.S. at 514. In *44 Liquormart*, the Court rejected the proposition that the power to regulate commercial activity is greater than the power to ban truthful, non-misleading commercial speech. *Id.* at 511-12 ("The text of the First Amendment makes clear that the Constitution presumes that attempts to regulate speech are more dangerous than attempts to regulate conduct. . . . As a result, the First Amendment directs that government may not suppress speech as easily as it may suppress conduct. . . . ").

Recognizing that this Court rejected its argument in *44 Liquormart*, Petitioners rework their words and try again. Instead of asserting that the greater power to regulate conduct can justify restricting speech related to that conduct, Petitioners argue in this case that the speech restrictions are a condition on an exemption from regulating the conduct. This gets Petitioners no farther. FDAMA's restriction on advertisement and solicitation as a condition upon the alleged "exemption" violates the First Amendment.

The cases upon which Petitioners rely in support of the newly minted "relinquishment theory," *Dolan v. City of Tigard*, 512 U.S. 374 (1994) and *Pickering v. Board of Educ.*, 391 U.S. 563 (1968), do not support Petitioners' claim. *Dolan* raised no First Amendment issues, but was a Fifth Amendment case that held that the government may not require a person to give up the right to receive just compensation when property is taken for public use. 512 U.S. at 385. In *Pickering*, this Court held that "the theory that public employment which may be denied altogether may be subjected to any conditions, regardless of how unreasonable has been uniformly rejected." 391 U.S. at

568, *quoting* citing *Keyinshan v. Board of Regents*, 385 U.S. 589, 605-606 (1967). These cases do not save Section 353a.

CONCLUSION

For all the foregoing reasons, it is respectfully submitted that the judgment of the Ninth Circuit Court of Appeals be affirmed.

Respectfully Submitted,

HOWARD M. HOFFMANN
Counsel of Record
JASON T. LUNDY
DUANE MORRIS LLC
227 W. Monroe – Suite 3400
Chicago, Illinois 60606
312/499-6700
Attorneys for Respondents

(9)

No. 01-344

Supreme Court, U.S.
FILED
FEB 19 2002
CLERK

In the Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

REPLY BRIEF FOR THE PETITIONERS

THEODORE B. OLSON
Solicitor General
Counsel of Record
Department of Justice
Washington, D.C. 20530-0001
(202) 514-2217

ALEX M. AZAR, II
General Counsel
U.S. Department of Health and Human Services

DANIEL E. TROY
Chief Counsel
U.S. Food & Drug Administration
Washington, D.C. 20857

25pp

TABLE OF CONTENTS

	Page
1. Section 353a furthers substantial governmental interests	3
2. Section 353a directly and materially advances the government's interests	16
3. Section 353a is no more extensive than necessary to further the government's interests	17

TABLE OF AUTHORITIES

Cases:

Alberty Food Prods. v. *United States*, 194 F.2d 463 (9th Cir. 1952)	13
Baker v. *United States*, 932 F.2d 813 (9th Cir. 1991)	15
Cedars North Towers Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978)	9, 10
Central Hudson Gas & Elec. Corp. v. *Public Serv. Comm.*, 447 U.S. 557 (1980)	1, 16
Dolan v. *City of Tigard*, 512 U.S. 374 (1994)	20
44 Liquormart, Inc. v. *Rhode Island*, 517 U.S. 484 (1996)	18, 19, 20
International Union of Operating Eng'rs v. *Flair Builders, Inc.*, 406 U.S. 487 (1972)	8
Kadis v. *United States*, 373 F.2d 370 (1st Cir. 1967)	9
Lorillard Tobacco Co. v. *Reily*, 533 U.S. 525 (2001)	16
Marks v. *United States*, 310 F.2d 49 (5th Cir. 1962)	9
Pittsburgh Press Co. v. *Human Relations Comm'n*, 413 U.S. 376 (1973)	19

Case—Continued: Page

Posadas de Puerto Rico Assoc. v. *Tourism Co.*, 478 U.S. 328 (1986) 16
Professionals & Patients for Customized Care v. *Shalala*, 56 F.3d 592 (5th Cir. 1995) 10, 15
Rubin v. *Coors Brewing Co.*, 514 U.S. 476 (1995) 18, 19
Rush v. *United States*, 370 F.2d 520 (8th Cir. 1967) 9
United States v. *Algon Chem., Inc.*, 879 F.2d 1154 (3d Cir. 1989) 10, 13
United States v. *Arnold's Pharmacy*, 116 F. Supp. 310 (D. N. J. 153) 9
United States v. *Articles of Drug*, 625 F.2d 665 (5th Cir. 1980) 13
United States v. *Baxter Healthcare Corp.*, 712 F. Supp. 1352 (N.D. Ill. 1989) aff'd 901 F.2d 1401 (7th Cir. 1990) 13
United States v. *Carlisle*, 234 F.2d 196 (5th Cir. 1956) 9
United States v. *Dianovin Pharm., Inc.*, 475 F.2d 100 (1st Cir.), cert. denied, 414 U.S. 830 (1973) 15
United States v. *Edge Broad. Co.*, 509 U.S. 418 (1993) 16
United States v. *Gibson*, 135 F. Supp. 807 (E.D. Pa. 1955) 9
United States v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988) 10, 13
United States v. *Rutherford*, 442 U.S. 544 (1979) 13
United States v. *Sene X Eleemosynary Corp.*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983) 5, 9, 10
United States v. *Sullivan*, 332 U.S. 689 (1948) 9
Virginia State Bd. of Pharmacy v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976) 12, 18, 19
Weinberger v. *Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609 (1973) 11

Constitution, statutes and regulations: Page

U.S. Const. Amend. I 1, 19, 20
Act of June 25, 1938, ch. 675, § 291(p)(1), 52 Stat. 1041 11
Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 11
Federal Food Drug and Cosmetic Act, 21 U.S.C. 301 *et seq.* 1
21 U.S.C. 321(g)(1)(D) 14
21 U.S.C. 321(p)(1) 7, 8
21 U.S.C. 331(d) 12
21 U.S.C. 331(k) 14
21 U.S.C. 351(a)(2)(B) (1994 & Supp. V 1999) 14
21 U.S.C. 352(f) 14
21 U.S.C. 352(f)(1) 13
21 U.S.C. 353(b)(1)(B) (1994 & Supp. V 1999) 13
21 U.S.C. 353(b)(2) 13
21 U.S.C. 353a (Supp. V 1999) ..... *passim*
21 U.S.C. 353a(a) (Supp. V 1999) 1, 7
21 U.S.C. 353a(a)(2)(A) (Supp. V 1999) 14
21 U.S.C. 353a(c) (Supp. V 1999) 1, 19
21 U.S.C. 355 7
21 U.S.C. 355(a) 7, 12
21 U.S.C. 360(a)(1) 8
21 U.S.C. 360(b)-(d) 8
21 U.S.C. 360(g)(1) 8
21 U.S.C. 374(a)(2)(A) 8
21 U.S.C. 374(a)(1) 9
21 U.S.C. 501(a)(2)B 15
21 U.S.C. 505 15
21 U.S.C. 502(f)(1) 15

Statutes and regulations—Continued:

Mont. Code Ann. (2001):
§ 37-7-101(7) 5
§ 37-7-101(17) 5

Statutes and regulations—Continued:	Page
Ohio Rev. Code Ann. § 3715.01(14) (Anderson 2001)	5
Tex. Occ. Code Ann. (West 2001):	
§ 551.003(9)	5
§ 551.003(23)	5
21 C.F.R. 130.39 (1968)	12
21 C.F.R. (2001):	
Pt.:	
Section 201.5	13
Section 201.100 *et seq.*	14
Pt. 210	14
Pt. 211	14
Miscellaneous:	
ASHP Gears Up Multistate Action Plan Regarding Sterile Drug Products, 48 Am. J. Hosp. Pharm. 386 (1991)	4
J. Avorn, et al., *Scientific versus Commercial Source of Influence on the Prescribing Behavior of Physicians*, 73 Am. J. of Med. 4 (July 1982)	17
17 Fed. Reg. 6818 (1952)	13
33 Fed. Reg. 7758 (1968)	12
J. Feinberg, *Compounding Sterile Products: What is Good Pharmacy Practice?*, 7 The Consultant Pharmacist 1012 (1992)	4
H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. (1997)	15
R. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753 (1996)	11
NAPB, *The Model State Pharmacy Act and Model Rules of the NAPB* (1996)	5
J. O'Donnell, *Cardioplegia Litigation and Recommendations*, 6 J. Pharm. Practice 151 (1993)	4
S. Rep. No. 43, 105th Cong., 1st Sess. (1997)	15
L. Trissel, *Compounding Our Problems*, 51 Am. J. Hosp. Pharm. 1534 (1994)	4

In the Supreme Court of the United States

No. 01-344

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

REPLY BRIEF FOR THE PETITIONERS

The Food and Drug Administration Modernization Act of 1997 (FDAMA) creates a limited exemption from the requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, governing the approval of new drugs, adequate directions for use, and good manufacturing practice for drugs compounded by pharmacists. See 21 U.S.C. 353a (Supp. V. 1999). The exemption is contingent on the pharmacist's compliance with various conditions, including that the pharmacist not solicit prescriptions for, advertise, or promote any particular compounded drug or class of compounded drug. 21 U.S.C. 353a(a) and (c) (Supp. V 1999). That condition is consistent with the First Amendment under *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557 (1980).

Section 353a is designed to advance the substantial governmental interest in balancing two important but competing goals. The first goal is to safeguard the integrity of the FDCA's new drug approval process, which protects the public from the health risks of widespread distribution of drugs that have not been proven safe and effective. See Pet. Br. 19-23. The second is to make compounded drugs available when necessary to meet the particularized medical needs of individual patients. See *id.* at 23-26. Those goals are in tension with each other but that tension may be accommodated and reconciled: It typically is not feasible to subject drugs compounded by a pharmacy in response to individual medical needs to the expensive premarket approval process. *Id.* at 26-27. At the same time, a blanket exemption from that process for anyone holding a pharmacy license would undermine the process by allowing drugs to be mass-produced outside the stringent regulatory framework established by Congress, and, by thereby reducing the incentive for other manufacturers to establish the safety and effectiveness of their products. *Id.* at 28-29.

The solicitation and advertising conditions thus directly advance the government's interest in balancing those competing goals. Promotion of particular drugs reasonably distinguishes large-scale drug manufacturing, which can and should be subject to premarket approval, from compounding in response to the particularized medical needs of specific individuals. See Pet. Br. 32-35. Conditioning the exemption from the approval requirements on the absence of promotion of particular drugs also reflects the FDCA's underlying premise that the public health is best served when those who develop, promote, and mass-distribute new drugs prove that they are safe and effective. Because all persons who compound new drugs (whether traditional manufacturers or those holding a pharmacy license) are unable to promote specific products through advertising unless they comply

with the approval process, they are unable to take advantage of a mass-market without complying with the process. The integrity of the process and the incentive for drug manufacturers to prove that the drugs that they distribute in interstate commerce are safe and effective are thereby preserved. *Id.* at 35-36. The advertising and solicitation limitations are thus carefully crafted to meet the government's goals. See *id.* at 42-46.

1. Section 353a Furthers Substantial Governmental Interests

a. Respondents contend (Br. 18-23) that the government has not established a substantial interest in subjecting compounding that is tantamount to manufacturing to the new drug approval process. They first argue (Br. 18, 20-21) that the government has not adequately and properly delineated the difference between compounding and manufacturing. The government's opening brief, however, differentiates between the two processes in terms similar to those used by the National Association of Boards of Pharmacy (NABP) itself. See Pet. Br. 33-35 & n.6. Traditional compounding involves the provision of a service in response to a physician's prescription and the particular medical needs of an individual patient that cannot be met by commercially available products. *Id.* at 33. Because traditional compounding responds to idiosyncratic medical needs of specific individuals, advertising of particular compounded drug products is not one of its necessary or common characteristics. *Id.* at 33-34. Manufacturing, in contrast, is the large-scale production of a drug product, typically for a substantial market that can support the expense and other rigors of the premarket approval process. Because manufacturing involves creation of a homogenous product that addresses the shared medical need of a large group of people, advertising of that product is one of its common and typically critical features. See *id.* at 34-35.

Respondents argue (Br. 21-22, 30, 44) that the widespread distribution of unapproved compounded drugs is not harmful. The very premise of the FDCA, however, is that widespread distribution of drugs that have not been proven safe and effective poses substantial risks to public health and that premarket approval is necessary to protect against those risks. See Pet. Br. 23, 30. That premise is supported by many decades of experience showing that neither the self-interest of drug producers nor physician screening is sufficient to protect the public. See *id.* at 20-23. The widespread distribution of unapproved new drugs threatens the integrity of the drug approval process and the public health whether or not the manufacturer has a pharmacy license under state law. See *id.* at 27-29.[1]

Respondents (Br. 12, 20) and amicus National Community Pharmacists Association (NCPA) (Br. 24-25) also contend that advertising of particular drugs does not reasonably distinguish manufacturing from traditional compounding. As just described, however, promotion of the manufactured product is a common and typically critical feature of commercial drug manufacturing, but not of traditional compounding. Indeed, NABP's Model State Pharmacy Act distinguishes between manufacturing and compounding based on the presence or absence of promotional activity. Compare § 105(u) (defining "manufacturing" to include "the promotion and

[1] Although respondents assert (Br. 30) that the government has offered only "one anecdotal incident" documenting the health risks from drugs compounded by pharmacists, the articles cited in the government's opening brief (at 28) discuss several incidents, and there is ample additional documentation of these risks. See, *e.g.*, *ASHP Gears Up Multistep Action Plan Regarding Sterile Drug Products*, 48 Am. J. Hosp. Pharm. 386 (1991); J. Feinberg, *Compounding Sterile Products: What is Good Pharmacy Practice?*, 7 The Consultant Pharmacist 1012, 1013 (1992); J. O'Donnell, *Cardioplegia Litigation and Recommendations*, 6 J. of Pharm. Practice 151, 151-152 (1993); L. Trissel, *Compounding Our Problems*, 51 Am. J. Hosp. Pharm. 1534 (1994).

marketing" of drugs) with § 105(e) (omitting promotion and marketing from definition of compounding) (*reprinted in* NABP, *The Model State Pharmacy Act and Model Rules of the NABP* 1.2, 1.4 (1996)). Many state laws draw a similar distinction. See Am. Pharm. Ass'n (APhA) Amicus Br. 15 n.19 (citing 10 state statutes); Mont. Code Ann. § 37-7-101(7) and (17) (2001); Ohio Rev. Code Ann. § 3715.01(14) (Anderson 2001); Tex. Occ. Code Ann. § 551.003(9) and (23) (West 2001). Moreover, the NABP's *Good Compounding Practices Applicable to State Licensed Pharmacies* prohibit a pharmacist from soliciting prescriptions for, advertising or otherwise promoting specific compounded drugs. NABP, *supra*, at App. C.2.

b. Respondents argue (Br. 12, 19-20, 29) that the government lacks a substantial interest in preventing manufacturing under the guise of pharmacy compounding because "compounding can never be manufacturing and manufacturing can never be compounding." *Id.* at 19. Respondents assert (*ibid.*) that pharmacy compounding differs from manufacturing because drugs compounded by pharmacists are dispensed directly to patients based on prescriptions arising from physician/patient/pharmacist relationships. Those characteristics do not, however, distinguish compounding from large-scale drug production that can and should be subject to premarket approval. Pharmacies (or traditional manufacturers that form entities with a pharmacy license) could still "compound" new drugs in the manner of traditional manufacturing even if they dispensed the drugs pursuant to patient prescriptions. In *United States* v. *Sene X Eleemosynary Corp.*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983), for example, the "pharmacy" dispensed the drugs it produced pursuant to prescriptions for individual patients. The court nonetheless concluded that the "pharmacy" was manufacturing, *id.* at 39,118, and respondents agree (Br. 41).

Under respondents' theory, nothing would prevent a "compounding pharmacy" from producing the next Prozac and marketing it nationwide to millions of individuals, without first proving the drug's safety and effectiveness to the FDA, provided only that the pharmacy made its sales pursuant to prescriptions mailed or telephoned in by physicians. Thus, respondents' approach would allow wholesale circumvention of the drug approval process and seriously undermine the FDCA's central mechanism to protect the public at large from the risks of drugs that have not been proven safe and effective.

Respondents assert, without support, that, "if and when demand for a compound ever increases to a level where manufacturing becomes practical (*i.e.*, profitable), a manufacturer may bring it to market, whereupon pharmacies will stop making it." Resp. Br. 19. If, however, pharmacies were already meeting the demand for a product through compounding, and doing so without bearing the costs of FDA approval, there would be little incentive for a prospective manufacturer to undertake the expense of obtaining FDA approval, particularly if pharmacies could sell the product at a lower price because they do not have to recoup the costs of the approval process. Further, if pharmacies knew that they could sell the drug at a lower price and thus enjoy an advantage over potential competitors, the pharmacies would be unlikely to give up their existing, profitable business.

c. Respondents and their amici proffer one additional reason why the government purportedly lacks a substantial interest in preventing circumvention of the new drug approval process: They assert that drugs compounded in the ordinary practice of pharmacy are not subject to the approval process in the first place and thus may legally be introduced into interstate commerce or held for sale without FDA approval. See Resp. Br. 3, 12-14, 16, 29, 34-45, 46; Amicus Br. of Int'l Academy of Comp. Pharm. (IACP) 2-22; NCPA Br. 10-15; APhA Br. 20-24.

i. As an initial matter, compounded drugs are not exempt from the new drug approval requirements. If they were, Congress would have had no need to create the exemption from those requirements that Section 353a provides. See 21 U.S.C. 353a(a) (Supp. V 1999) (stating that Section 355, which contains the approval requirements, "shall not apply" to compounded drugs under specified conditions). Thus, the enactment of Section 353a itself establishes that compounding by pharmacists is otherwise covered by the new drug approval requirements.

As explained in the government's opening brief (at 4), compounded drugs fall within the definition of a "new drug" in 21 U.S.C. 321(p)(1). They are thus subject to the approval requirements, which provide that "*[n]o person* shall introduce or deliver for introduction into interstate commerce *any new drug*" without prior FDA approval. 21 U.S.C. 355(a) (emphasis added). Neither respondents nor their amici identify any provision of the FDCA that exempts drugs compounded by pharmacies from the definition of new drug or the approval requirements.[2]

---

[2] Respondents incorrectly assert (Br. 12, 16, 34-35) that the government conceded in the court of appeals that introduction of compounded drugs into interstate commerce without FDA approval is legal. The government took the same position in that court that it takes here: Because Section 353a itself provides that introduction of compounded drugs into interstate commerce without FDA approval is legal under carefully circumscribed conditions, the government did not and does not argue that respondents' proposed advertisements of compounded drugs concern illegal activity under the first component of the *Central Hudson* test. See Pet. Br. 18; Appellants Br. 27 n.10. That does not mean, however, that introduction of unapproved compounded drugs into interstate commerce, or holding such drugs for sale, was legal before FDAMA, or is legal today absent compliance with the conditions in Section 353a. On the contrary, as the government's court of appeals' brief stated, "before

Respondents argue that compounded drugs are not "mentioned or included in" the definition of "new drug." Br. 4; see *id.* at 35, 37, 39. That definition, however, includes "*[a]ny* drug" that "is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use." 21 U.S.C. 321(p)(1) (emphasis added). The use of the modifier "any" eliminates the need explicitly to include drugs compounded by pharmacists. See *International Union of Operating Eng'rs* v. *Flair Builders, Inc.*, 406 U.S. 487, 491 (1972). Respondents do not contend that compounded drugs are generally recognized among experts as safe and effective. Indeed, respondents argue (Br. 35-37) that compounded drugs are not new drugs precisely because they are (according to respondents) incapable of being evaluated by experts. That fact, if true, however, demonstrates the opposite proposition—that compounded drugs necessarily are "new drugs."

ii. Respondents also argue more broadly (Br. 4, 8, 13, 37-40) that pharmacies are entirely exempted from the FDCA by 21 U.S.C. 360(a)(1), 360(g)(1), and 374(a)(2)(A). Section 360(a)(1), however, provides no exemption from any provision of the FDCA for any entity. Rather, it stipulates that repackaging or relabeling constitutes "manufacture, preparation, propagation, compounding, or processing" that generally subjects the person engaged in such conduct to the registration requirements contained in Section 360(b)-(d). Section 360(g)(1) exempts pharmacies that engage in only the ordinary pharmacy practice of dispensing or selling drugs at retail from registration requirements, and Section 374(a)(2)(A) exempts such pharmacies from certain (but not

---

Congress enacted FDAMA in 1997, the FDCA did not exempt compounding from the Act's new drug, adulteration, and misbranding requirements," *id.* at 27, and "the interstate distribution of any compounded drug product without approval was illegal." *Id.* at 31.

all) of the inspection requirements in Section 374(a)(1). Those provisions do not, however, exempt pharmacies from any *other* provisions of the FDCA, including those governing new drug approval, misbranding, and adulteration. Pet. Br. 3. Indeed, the existence of express exemptions from the registration and inspection requirements confirms that pharmacies are generally subject to the FDCA and that they are *not* exempt (except to the extent expressly provided in Section 353a) from those other requirements.

iii. Respondents claim that the FDA has demonstrated a "complete lack of regulation or enforcement activity towards pharmacies." Br. 14. That claim cannot be reconciled with *United States* v. *Sullivan*, 332 U.S. 689 (1948), in which this Court upheld a misbranding action brought against a pharmacist less than a decade after the FDCA was enacted. See also *Kadis* v. *United States*, 373 F.2d 370 (1st Cir. 1967); *Rush* v. *United States*, 370 F.2d 520 (8th Cir. 1967); *Marks* v. *United States*, 310 F.2d 49 (5th Cir. 1962); *United States* v. *Carlisle*, 234 F.2d 196 (5th Cir. 1956); *United States* v. *Gibson*, 135 F. Supp. 807 (E.D. Pa. 1955); *United States* v. *Arnold's Pharmacy*, 116 F. Supp. 310 (D.N.J. 1953). As described in the 1992 Compliance Policy Guide (CPG) on compounding, the FDA has long taken the position that drugs compounded by pharmacies are subject to the new drug approval requirements. See Pet. Br. 4-5; Pet. App. 71a, 72a (CPG). Respondents and some amici mistakenly contend (Resp. Br. 25, 43; ICPA Br. 5, 14; NCPA Br. 12) that the FDA had not taken that position before promulgating the CPG. The FDA made clear that compounded drugs are new drugs and subject to the approval requirements many years before the 1992 CPG. See Pet. App. 74a; Pet. Br. 6 (citing *Sene X* and *Cedars North Towers Pharmacy, Inc.* v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,828 (S.D. Fla. Aug. 28, 1978), in which the FDA successfully contended that drugs com-

pounded by pharmacists were subject to the approval requirements).

The government's position that compounded drugs are subject to the new drug approval requirements is supported by lower court decisions rendered well before FDAMA confirmed that coverage in 1997. See Pet. Br. 5, 6 (citing cases). Respondents and their amici (Resp. Br. 40-42; APhA Br. 17-20; IACP Br. 5 n.4; NACP Br. 12 n.44) attempt to distinguish those cases on various grounds. The facts remain, however, that, in two of the cases, the courts held that drugs compounded by pharmacies were new drugs subject to the approval process. *Sene X*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207, at 39,118; *Cedars North Towers Pharmacy*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,827. In two others, the courts held that bulk drugs intended for use in compounding by veterinarians were not covered by a regulatory exception from the FDCA's misbranding provisions because the compounded drugs would be "new drugs" for which the veterinarians had not filed approval applications. *United States* v. *Algon Chem., Inc.*, 879 F.2d 1154, 1158 (3d Cir. 1989); *United States* v. *9/1 Kg. Containers*, 854 F.2d 173, 178 (7th Cir. 1988). And, in a fifth case, the court stated that the FDCA "does not expressly exempt 'pharmacies' or 'compounded drugs' from the new drug, adulteration, or misbranding provisions." *Professionals & Patients for Customized Care* v. *Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995). Respondents and their amici, on the other hand, cite no case holding that drugs compounded by pharmacists are not "new drugs" or that they are exempt from the approval requirements, and we are aware of none.

iii. Respondents' amici contend that Congress could not have subjected compounded drugs to the approval process because that would have been "tantamount to the outlawing

of compounding." APhA Br. 22; see also Resp. Br. 36-37; IACP Br. 3-4. They argue that Congress would not have outlawed compounding when it enacted the FDCA in 1938 because most prescriptions at that time required compounding. APhA Br. 21-22; IACP Br. 11; NCPA Br. 8, 11-13. That argument rests on the mistaken premise that, if all drugs compounded by pharmacists are new drugs under the current version of the FDCA, then all compounded drugs must also have been new drugs under the FDCA as enacted in 1938. In fact, most compounded drugs would not have been "new drugs" under the definition in the 1938 Act. That definition excluded drugs that had been marketed before 1938 and did not classify a drug as a "new drug" based on lack of general recognition of its effectiveness. See Act of June 25, 1938, ch. 675, § 201(p)(1), 52 Stat. 1041; Pet. Br. 21; *Weinberger* v. *Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609, 630 (1973). In addition, the 1938 Act was understood to permit the manufacture and marketing without approval of drugs similar to approved drugs in reliance on an approved "pioneer" drug application, and the FDA often issued advisory opinions that such products were not new drugs. See *id.* at 614; R. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753, 1772 (1996) (estimating that nearly 40,000 drugs similar to 4000 approved drugs were marketed without formal FDA approval before 1962).

In 1962, Congress expanded the scope of the new drug approval requirements by, among other things, expanding the definition of "new drug" to encompass drugs not generally recognized as effective for the uses prescribed, recommended, or suggested in their labeling, and requiring effectiveness to be established for each use of a new drug before the drug can be marketed for that use. See Pub. L. No. 87-781, 76 Stat. 780; Pet. Br. 22-23. In 1968, in response to the 1962 amendments, the FDA stopped providing informal

opinions that unapproved products were not new drugs, revoked all previously issued opinions, and made clear that changes "in formulation, manufacture, control, or labeling" may render a product a new drug. See 33 Fed. Reg. 7758 (1968) (codified at 21 C.F.R. 130.39 (1968)). As a result, most compounded drugs were not new drugs subject to premarket approval until the mid-1960s. By that time, less than five percent of prescriptions involved compounding. See NCPA Br. 8; *Virginia State Bd. of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 753, 766 (1976) (estimating that the same percentage of prescriptions involved compounding in the mid-1970s). Shortly thereafter, and well before FDAMA was enacted, the FDA took formal enforcement action against some pharmacies based on failure to comply with the new drug approval requirements. See p. 9, *supra*.

The compounding and sale of new drugs by pharmacies triggered the application of the FDCA in several ways under the Act as it then existed. First, the FDCA prohibits the "introduction or delivery for introduction into interstate commerce" of any "new drug," unless it is covered by an approved new drug application. 21 U.S.C. 331(d), 355(a). Whether a local pharmacist's dispensing of a compounded drug entails or causes "introduction or delivery for introduction into interstate commerce" depends on the particular circumstances. It was less likely to do so in the middle of the 20th century, when interstate commerce was far less extensive than it is today. Respondents, however, are not the prototypical "local" pharmacist; between 60% and 95% of respondents' total sales of compounded drugs are to out-of-state customers. See Compl. ¶ 26 (C.A.E.R. 7).

Because pharmacies likewise are not exempt from the FDCA's misbranding and adulteration provisions, those provisions also applied to compounding by pharmacies. Compounded drugs of the sort traditionally created by pharmacies are prescription drugs. The FDA has interpreted the FDCA to provide that all unapproved prescription drugs are misbranded, and the lower courts have sustained that interpretation. See, *e.g.*, *United States* v. *Articles of Drug*, 625 F.2d 665, 673, 675 (5th Cir. 1980); *United States* v. *Baxter Healthcare Corp.*, 712 F. Supp. 1352, 1359 (N.D. Ill. 1989), aff'd, 901 F.2d 1401 (7th Cir. 1990); see also *Algon Chem.*, *supra* (applying this interpretation to bulk drugs to be used as components of compounded veterinary drugs); *9/1 Kg. Containers*, *supra* (same).

Under 21 U.S.C. 352(f)(1), a drug is misbranded unless its labeling bears "adequate directions for use," which the FDA has long defined to mean "directions under which the layman can use a drug safely and for the purposes for which it is intended." See 17 Fed. Reg. 6818 (1952) (promulgating 21 C.F.R. 201.5); *Alberty Food Prods.* v. *United States*, 194 F.2d 463, 464 (9th Cir. 1952). The FDA has determined that directions under which the layperson can use a drug safely cannot be written for an *approved* prescription drug because such drugs, by definition, are "not safe for use except under the supervision of a practitioner licensed by law to administer" them, 21 U.S.C. 353(b)(1)(B) (1994 & Supp. V 1999), and are therefore unsuitable for self-medication. See *Articles of Drug*, 625 F.2d at 672-673. In the case of *unapproved* new drugs, adequate directions for use cannot be written as a matter of law, even by a physician. See *Algon Chem.*, 879 F.2d at 1159-1161 (explaining that the FDCA was intended to control the availability of drugs for prescribing by physicians, and prescriptions for compounded drugs that are unapproved new drugs are not exempted from the Act as an aspect of the practice of medicine) (citing *United States* v. *Rutherford*, 442 U.S. 544 (1979)); *9/1Kg. Containers*, 854 F.2d at 176-177 (also citing *Rutherford*).[3]

---

[3] The FDCA provides an exemption from the requirement that drugs contain adequate directions for use for "[a]ny drug dispensed by filling or

In addition, before enactment of FDAMA, compounded drugs and their components often would have been considered adulterated under the FDCA, because a drug is adulterated whenever it is "manufacture[d], process[ed], pack[ed], or h[eld]" under methods, facilities or controls that "do not conform to or are not operated or administered in conformity with current good manufacturing practice." 21 U.S.C. 351(a)(2)(B) (1994 & Supp. V 1999). FDA regulations (21 C.F.R. Parts 210 and 211) establish the minimum requirements. Because those requirements were stringent, especially as they developed over time, compliance with them was costly, and most pharmacy compounding processes and facilities would not have complied.

The FDCA prohibits "the doing of any * * * act with respect to, a * * * drug * * *, if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such article being adulterated or misbranded." 21 U.S.C. 331(k). The definition of drug includes not only the finished product itself, but also its components. 21 U.S.C. 321(g)(1)(D). Thus, if a drug or one of its components had been shipped in interstate commerce, and the drug or its components became adulterated or misbranded while the drug or the components were held for sale after that shipment, Section 331(k) was

---

refilling a written or oral prescription of a practitioner licensed by law to administer such drug." 21 U.S.C. 353(b)(2). That exemption, however, applies only at the time the drug is "dispensed." Thus, when compounded drugs are prepared in advance of dispensing, for example "in limited quantities before the receipt of a valid prescription order for such individual patient," 21 U.S.C. 353a(a)(2)(A) (Supp. V 1999), they lack adequate directions for use, and thus are misbranded unless they qualify for a regulatory exemption from the adequate-directions-for-use requirement. See 21 U.S.C. 352(f) (authorizing Secretary to exempt drugs from that requirement); 21 C.F.R. 201.100 *et seq.* (exemptions). Unapproved new drugs that are not intended solely for investigational use do not qualify for any of the regulatory exemptions. See *ibid.*

violated. See, *e.g.*, *Baker* v. *United States*, 932 F.2d 813, 814-815 (9th Cir. 1991); *United States* v. *Dianovin Pharm., Inc.*, 475 F.2d 100, 103 (1st Cir.), cert. denied, 414 U.S. 830 (1973).

It was against the background of those statutory provisions and the FDA announcement and implementation of its enforcement policy in 1992 (see Pet. App. 71a; *Professionals & Patients*, 56 F.3d at 593-594, 599) that Congress enacted Section 353a to specify in the FDCA itself the circumstances in which compounding by pharmacists would be lawful under the FDCA. Section 353a reflected "extensive" consultation by committees of Congress with the FDA and other interested parties to reach a consensus on how "to ensure the continued availability of compounded drugs as a component of individualized therapy, while limiting the scope of compounding to prevent manufacturing under the guise of compounding." H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. 94 (1997); accord S. Rep. No. 43, 105th Cong., 1st Sess. 67 (1997). As enacted by Congress, Section 353a responds to the application of the new drug approval, misbranding, and adulteration provisions of the FDCA, as described above, by exempting pharmacy compounding from Sections 355 (new drug approval), 352(f)(1) (adequate directions for use) and 351(a)(2)(B) (good manufacturing practice) of Title 21 if the compounding complies with the conditions in Section 353a.

iv. Even if drugs compounded in the ordinary practice of pharmacy were exempt from the premarket approval requirements, the government still would have a substantial interest in preventing abuse of that exemption by pharmacies engaged in compounding that *exceeds* the ordinary practice of pharmacy and is tantamount to manufacturing. Pharmacies that engage in such activity directly circumvent the new drug approval process and undermine the incentives for traditional manufacturers to comply with that process. Section 353a's solicitation and advertising conditions are well

calibrated to that interest, because a pharmacy that is compounding without complying with those conditions is not engaged in the ordinary practice of pharmacy, which as described above, does not include advertising or promoting particular compounded drugs. See pp. 3, 4-5, *supra*.

2. Section 353a Directly And Materially Advances The Government's Interests

Respondents contend (Br. 25-32) that Section 353a does not directly and materially advance the government's interests. Much of respondents' argument (Br. 26-29, 30-32) is devoted to demonstrating that Section 353a does not advance a supposed governmental interest in reducing demand for compounded drugs. The government's interest is *not*, however, in suppressing demand for compounded drugs. See Pet. Br. 38. The government's interest is in balancing the competing goals of protecting the integrity of the drug approval process and preserving the availability of compounding by pharmacists in response to individual medical needs. Thus, the government seeks to ensure that a compounded drug is subjected to premarket approval when demand is or may be widespread and advertising could channel demand to that unapproved new drug.

Respondents' arguments that advertising does not drive demand for compounded drugs because physicians act as a brake (Br. 28), that advertising generally only channels and does not create demand (Br. 29), and that this Court and other courts have rejected prohibitions on advertising as a means of suppressing demand (Br. 26-28) are thus beside the point. In any event, there is support in this Court's cases for the common-sense proposition that advertising stimulates demand as well as channels it. See *Lorillard Tobacco Co.* v. *Reilly*, 533 U.S. 525 (2001); *Central Hudson*, 447 U.S. at 567-569; *United States* v. *Edge Broad. Co.*, 509 U.S. 418, 434 (1993). *Posadas de Puerto Rico Assoc.* v. *Tourism Co.*, 478 U.S. 328, 341-342 (1986). This common-sense proposition

would seem to apply to physicians as well. J. Avorn, *et al.*, *Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians*, 73 Am. J. of Med. 4, 6 (July 1982) ("Physicians who held advertising-oriented beliefs about the index drugs were generally unaware that they were strongly influenced by non-scientific sources.").

The FDAMA provisions that respondents assert undermine the government's interest (Br. 30-32) do not undermine the government's *actual* interest in preventing manufacturing of unapproved new drugs under the guise of compounding. FDAMA permits a pharmacy to advertise its compounding services generally because that kind of advertising does not suggest the existence of, or foster the growth of, a market for any *particular* compounded drug. Such advertising therefore does not distort the incentives of drug manufacturers to comply with the new drug approval provisions. At the same time, advertising of compounding services promotes the governmental interest in preserving the availability of pharmacy compounding in response to individual medical needs. Pet. Br. 40. Likewise, the absence of more stringent volume limitations on the *aggregate* distribution of compounded drugs does not undermine the advertising and solicitation provisions, which are designed to prevent compounding without premarket approval of a *particular* drug that is tantamount to manufacturing. *Id.* at 41.

3. Section 353a Is No More Extensive Than Necessary To Further The Government's Interests

Respondents also contend (Br. 13, 32-33) that Section 353a's advertising and solicitation provisions are more extensive than necessary to accomplish the government's aims. Respondents argue (Br. 32-33) that disclaimers could prevent consumers from being misled into believing that compounded drugs are FDA-approved. They do not explain, however, how disclaimers are consistent with the goal of

preserving the integrity of the new drug approval provisions. Instead, respondents suggest (Br. 13) that the government's concern about the new drug approval process is misplaced because compounded drugs are not subject to preapproval. As discussed above, however, that suggestion is incorrect. See pp. 6-15, *supra*. Respondents' contention (Br. 44) that a physician prescription provides adequate protection for patients who receive compounds suffers from a similar flaw. The very premise of the FDCA, based on decades of experience, is that physician screening is not sufficient to protect against the risks of widespread distribution of drugs that have not been proven safe and effective. See Pet. Br. 20-23.

Respondents suggest (Br. 45) that Section 353a's advertising and solicitation provisions are unnecessary to safeguard the new drug approval process because the FDA can take enforcement action against a pharmacy that threatens that process by operating beyond the ordinary practice of pharmacy. According to the NABP itself, however, solicitation or advertising of specific compounded drugs *is* activity outside the ordinary practice of pharmacy. See p. 5, *supra*. Moreover, the FDA historically considered whether a pharmacy was engaging in promotional activity in determining whether the pharmacy was exceeding the bounds of ordinary pharmacy practice. Pet. Br. 6, 32-33.

Respondents also incorrectly contend that the solicitation and advertising provisions are more extensive than necessary because they are "absolute restrictions upon truthful speech" and "prevent the very types of advertisement and promotion that this Court held could not be restricted in other cases." Resp. Br. 33 (citing *44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484 (1996), *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476 (1995), and *Virginia State Bd. of Pharmacy*, *supra*). Section 353a does *not* absolutely prohibit any speech. A pharmacy that wishes to mass-produce a particular drug and promote that product by advertising may do so—just as any other manufacturer may—if it complies with the FDCA's new drug approval and related requirements. It is only if the pharmacy desires to avail itself of the exemption from those otherwise generally applicable requirements that it must limit its promotional activities. Moreover, even when a pharmacy takes advantage of the exemption, it is permitted to advertise its compounding services generally. 21 U.S.C. 353a(c) (Supp. V 1999). Section 353a's advertising and solicitation provisions are thus significantly less onerous than the absolute prohibitions on speech involved in *44 Liquormart*, 517 U.S. at 489-490 (categorical ban on advertisement of alcohol prices); *Coors Brewing*, 514 U.S. at 480-481 (prohibition on disclosure of alcohol content on beer labels); and *Virginia State Board of Pharmacy*, 425 U.S. at 752 (effective prohibition on advertising or other affirmative dissemination of all prescription drug price information).

Finally, respondents contend (Br. 46-48) that, even if compounded drugs are subject to the new drug approval requirements, the First Amendment categorically prohibits conditioning an exemption from such a generally applicable requirement on relinquishment of First Amendment rights. But, to the extent that pharmacy compounding violated the FDCA before FDAMA was enacted (see pp. 12-15, *supra*), respondents had no First Amendment right to advertise the sale of compounded drugs. See *Pittsburgh Press Co.* v. *Human Relations Comm'n*, 413 U.S. 376, 388 (1973). They therefore were not required to relinquish any First Amendment right in exchange for the benefit of the exemption.

In any event, respondents' contention is not correct. Respondents rely on the plurality opinion in *44 Liquormart*. See Resp. Br. 46-47 (citing 517 U.S. at 510-514 (opinion of Stevens, J., joined by Kennedy, Thomas, and Ginsburg, JJ.)). That opinion, however, did not state that the government

may *never* condition an exemption from a generally applicable requirement on the beneficiary's agreement to a speech limitation. The opinion merely rejected the argument that the "greater" power to deny the exemption altogether *always* legitimizes the "lesser" power to condition the exemption on the surrender of First Amendment rights. See 517 U.S. at 510-513. Such a condition is subject to scrutiny under the Court's unconstitutional conditions doctrine, but that scrutiny is no more demanding than the *Central Hudson* test. See *Dolan* v. *City of Tigard*, 512 U.S. 374, 385, 391 (1994) (noting that government may not condition benefit on relinquishment of a constitutional right unless waiver of right is reasonably related to benefit and citing First Amendment cases). As explained above and in our opening brief, the solicitation and advertising condition on the exemption provided by Section 353a satisfies scrutiny under *Central Hudson*.

* * * * *

For the foregoing reasons, and the reasons stated in our opening brief, the judgment of the court of appeals should be reversed, and the case should be remanded with instructions to enter judgment for the petitioners.

Respectfully submitted.

THEODORE B. OLSON
Solicitor General

ALEX M. AZAR, II
General Counsel
U.S. Department of Health and Human Services

DANIEL E. TROY
Chief Counsel
U.S. Food & Drug Administration

FEBRUARY 2002

No. 01-344

FILED

JAN 11 2002

IN THE

Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES, *et al.*,
Petitioners,

v.

WESTERN STATES MEDICAL CENTER, *et al.*,
Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Ninth Circuit

AMICI CURIAE BRIEF OF JULIAN M. WHITAKER, M.D.; AMERICAN ASSOCIATION FOR HEALTH FREEDOM; DURK PEARSON; SANDY SHAW; PURE ENCAPSULATIONS, INC.; WELLNESS LIFESTYLES, INC. D/B/A AMERICAN LONGEVITY; HERO NUTRITIONALS, INC.; LIFE SERVICES SUPPLEMENTS, INC.; LIFE ENHANCEMENT PRODUCTS, INC.; AND LIFE EXTENSION FOUNDATION, SUPPORTING RESPONDENTS

JONATHAN W. EMORD *
CLAUDIA A. LEWIS-ENG
ANDREA G. FERRENZ
EMORD & ASSOCIATES, P.C.
5282 Lyngate Court
Burke, VA 22015
(202) 466-6937
Attorney for Amici Curiae

* Counsel of Record

January 11, 2002

WILSON-EPES PRINTING CO., INC. – (202) 789-0096 – WASHINGTON, D. C. 20001

BEST AVAILABLE COPY

TABLE OF CONTENTS

	Page
TABLE OF AUTHORITIES	iii
INTEREST OF THE *AMICI CURIAE*	1
SUMMARY OF ARGUMENT	2
ARGUMENT	7
I. HEALTH AND SAFETY REGULATION OF COMPOUNDING HAS LONG BEEN A STATE PROVINCE	7
A. The Historic and Indispensable Role of Compounding	8
B. Modern State Regulation of Compounding	13
II. CONGRESSIONAL AND FDA RECOGNITION AND ACCEPTANCE OF STATE COMPOUNDING REGULATION	16
III. COMPOUNDING IS BUT ONE OF SEVERAL EXEMPTIONS FROM THE FDCA'S DRUG APPROVAL PROCESS	17
A. The Statutory and Regulatory Exemptions from New Drug Approval	18
1. Personal Use Importation of Unapproved Drugs	18
2. Unapproved Uses of Approved Drugs	18
3. Investigational Use of Drugs	20
B. FDA's pre-FDAMA Limits on Substances Used in Compounding and on Interstate Distribution of Compounded Drugs	20

TABLE OF CONTENTS—Continued

Page

C. The Non-Speech Provisions of the FDCA, Left Unchallenged in This Litigation, Have Been Construed to Permit Regulation of the Amount of Compounding and, To a Large Extent, the Availability of Substances for Compounding ... 20

IV. THE POWER TO REGULATE COMPOUNDING DOES NOT INCLUDE THE POWER TO REGULATE TRUTHFUL AND NONMISLEADING ADVERTISING 21

V. THE GOVERNMENT'S JUSTIFICATION FOR BANNING ADVERTISING OF SPECIFIC COMPOUNDED DRUGS AND PRICES, BUT NOT OF THE AVAILABILITY OF COMPOUNDING SERVICES, LACKS RATIONALITY AND FAILS THE DIRECT AND MATERIAL ADVANCEMENT TEST 24

VI. THERE ARE NUMEROUS AND OBVIOUS LESS RESTRICTIVE NON-SPEECH REGULATORY ALTERNATIVES TO THE GOVERNMENT'S SPEECH BAN 25

VII. SEVERAL LOWER FEDERAL COURT CASES REVEAL THE FDAMA SPEECH BAN TO BE PART OF A GENERAL FDA PATTERN OF SPEECH SUPPRESSIVE ACTIONS, ALL DIRECTLY INFLUENCED BY THE COURT'S RESOLUTION OF THE FIRST AMENDMENT ISSUE IN THIS CASE 27

CONCLUSION 28

TABLE OF AUTHORITIES

CASES Page

44 Liquormart v. Rhode Island, 517 U.S. 484 (1996) 4, 21, 22, 26

Bates v. State Bar of Arizona, 433 U.S. 350 (1977) 22, 26

Central Hudson Gas & Electric Corporation v. Public Service Commission of New York, 447 U.S. 557 (1980) 6, 7, 26

Chaney v. Heckler, 718 F.2d 1174 (D.C. Cir. 1983) 3, 17

Cowan v. United States, 5 F. Supp. 2d 1235 (N.D. Okla. 1998) 16, 17, 19

Edenfield v. Fane, 507 U.S. 761 (1993) 6, 26

Frost & Frost Trucking Company v. Railroad Commission of California, 271 U.S. 583 (1926) 22

Ibanez v. Florida Department of Business and Professional Regulation, 521 U.S. 136 (1994) .. 6

In re RMJ, 455 U.S. 191 (1982) 26

Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999); *reh'g denied en banc*, 172 F.3d 72 (D.C.Cir. 1999) 2, 7, 26, 27

Pearson v. Shalala, 130 F. Supp. 2d 105 (D.D.C. 2001) 2, 7, 26, 27

Pearson v. Thompson, 141 F. Supp. 2d 105 (D.D.C. 2001) 2, 7, 26, 27

Peel v. Attorney Registration & Disciplinary Comm'n of Illinois, 496 U.S. 91 (1990) 26

Perry v. Sindermann, 408 U.S. 593 (1972) 22

Professionals & Patients for Customized Care v. Shalala, 487 F. Supp. 1359 (S.D. Tex. 1994) 8

Rubin v. Coors Brewing Company, 514 U.S. 476 (1995) 5, 6, 24, 25

TABLE OF AUTHORITIES—Continued

Page

United States of America v. Algon Chemical, Incorporated, 879 F.2d 1154 (3rd Cir. 1989).... 17, 19
United States v. Evers, 643 F.2d 1043 (5th Cir. 1981)..... 19
Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748 (1976).....2, 13, 22, 23
Washington Legal Foundation v. Henney, 56 F. Supp.2d 81 (D.D.C. 1999) *rev'd* 202 F.3d 331 (D.C.Cir. 2000)..... 26, 27
Zauderer v. Office of Disciplinary Counsel of Supreme Court of Ohio, 471 U.S. 626 (1985)... 6

CONSTITUTION, STATUTES, AND REGULATIONS

FDA Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997)..... *passim*
Food, Drug and Cosmetic Act (FDCA) § 501, 21 U.S.C. § 351 (2001)..... 4
FDCA § 502, 21 U.S.C. § 352 (2001)..... 18
FDCA § 503, 21 U.S.C. § 353 (2001)..... 16, 20
FDCA § 505, 21 U.S.C. § 355 (2001).....4, 18, 20
FDCA § 510, 21 U.S.C. § 360 (2001)..... *passim*
FDCA § 704, 21 U.S.C. § 374 (2001)..... 3, 18
All 50 States Medical Practice Acts Cited..... 5, 16
All 50 States Pharmacy Practice Acts Cited..... 13, 14
Md. Code Ann. Health Occupations § 12-101 (2001)..... 15
21 C.F.R. § 312 (2001)..... 18, 20

TABLE OF AUTHORITIES—Continued

Page

Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16,503 (1972)..... 19

MISCELLANEOUS

Allen, Jr., Ph.D., Loyd V., *Allen's Compounded Formulations: The U.S. Pharmacist Collection, 1995-1998* (1997)..... 11, 13
Allen, Jr., Ph.D., Loyd V., *The Art, Science, and Technology of Pharmaceutical Compounding* (1998).....8, 10, 11, 12
American Academy of Pediatrics, *Few Prescription Drugs Labeled for Pediatric Use*, ¶ 1, 3 (visited Dec. 20, 2001) <http://www.babybag.com/articles/aap_drug.htm>..... 19
Compounding for a Diverse Ambulatory Patient Base, 1 International Journal of Pharmaceutical Compounding 6 (1997)..... 11
Compounding for Hospice and Cancer Patients, 4 International Journal of Pharmaceutical Compounding 4 (2000)..... 11, 12
Compounding for Pain Management, 2 International Journal of Pharmaceutical Compounding 2 (1998)..... 11
Compounding for Pain Management, 4 International Journal of Pharmaceutical Compounding 1 (2000)..... 11
Compounding for Pediatric Patients, 5 International Journal of Pharmaceutical Compounding 1 (2001)..... 12

TABLE OF AUTHORITIES—Continued

	Page
Compounding Parenteral Nutrition Solutions, 2 International Journal of Pharmaceutical Compounding 5 (1998)	11
Duffy, John, *From Humors to Medical Science: A History of American Medicine* (1993)	10
Exodus 30:25	8
Exploring Compounding Options for Geriatric Patients, 1 International Journal of Pharmaceutical Compounding 3 (1997)	12
FDA, *Compliance Policy Guides*, § 460.200 (CPG 7132.16)(1992); Rescinded, 64 Fed. Reg. 1, 207 (1999)	*passim*
FDA, *Compliance Policy Guides*, 7125.40 Chap. 6 § 608.400 (2001)	17
FDA, *Regulation Procedures Manual*, "Coverage of Personal Importation," Chapter 9, (August 1997)	18
Gill, Jr., Harold B., *The Apothecary in Colonial Virginia* (1972)	9, 10
H.R. Rep. No. 74-2755 (1936)	19
Kremers, E. and Urdang, G., *History of Pharmacy: A Guide and a Survey* (1947)	8, 10
Kurland, *Posadas de Puerto Rico v. Tourism Company: "'Twas Strange, 'Twas Passing Strange; 'Twas Pitiful, 'Twas Wondrous Pitiful,"* 1986 S.Ct.Rev. 1, 12-15	21
LaWall, Charles, *The Curious Lore of Drugs and Medicines* (1927)	8, 10
Nightingale, M.D., Stuart L., *Use of Drugs for Unlabeled Indications*, FDA Perspective 269 (September 1986)	18, 19

TABLE OF AUTHORITIES—Continued

	Page
Nightingale, M.D., Stuart L., *Unlabeled Uses of Approved Drugs*, 26 Drug Information Journal 141 (1992)	18, 19
S. Rep. No. 105-43 (1997)	7, 27
S. Rep. No. 87-1744 (1962)	19
S. Rep. No. 74-361 (1935)	19
S. Rep. No. 74-646 (1935)	19
Troy, Daniel, *The FDA and Off-Label Uses of Drugs and Devices*, ¶ 3 (visited Dec. 20, 2001) <http://www.mediainst.org/digest/97fall/wlf.html>	19
United States Pharmacopoeial Convention, Inc., *United States Pharmacopoeia XXV/ National Formulary XX.* (2002)	13

INTEREST OF THE *AMICI CURIAE* [1]

Julian M. Whitaker, M.D. is a physician licensed to practice medicine in California and Washington. Dr. Whitaker prescribes compounded drugs for special needs patients. The petitioners prohibit advertising of compounded drug availability and price. Dr. Whitaker relies on that information to obtain for those patients competitively priced compounded drugs as efficiently as possible. He is therefore adversely affected, as are his patients, by the petitioners' advertising ban.

American Association for Health Freedom ("AAHF") is a Virginia non-profit corporation with over 500 physician, pharmacist, chiropractor and other health care practitioner members. AAHF endeavors to protect consumer access to preventive therapies and the right of health care providers to offer those therapies. AAHF's 240 physician members, including its nine physician board members, rely on the compounding services of pharmacists from across the nation. The drug price advertising the petitioners prohibit is precisely the advertising those members need most to provide their special needs patients competitively priced compounded drugs as efficiently as possible. Thus, AAHF's physician board members and physician members are adversely affected, as are their patients, by the petitioners' advertising ban.

Durk Pearson; Sandy Shaw; Pure Encapsulations, Inc.; Wellness Lifestyles, Inc. d/b/a American Longevity; Hero Nutritionals, Inc.; Life Enhancement Products, Inc.; Life

---

[1] Counsel of record for the *amici curiae* authored this brief in whole. The *amici curiae* paid all costs associated with the preparation and submission of the brief with the exception of a monetary contribution made by Coastal Georgia Health Institute, Inc., 158 Scranton Connector Blvd., Brunswick, GA 31525. The *amici* have received the written consent for the filing of this brief from counsel to the petitioners and the respondents. Those letters have been filed with the Clerk of the Court.

Extension Foundation; and Life Services Supplements, Inc. design, license and sell dietary supplements. As such, they are regulatees of the Food and Drug Administration (FDA). Their products labeling and advertising is directly (in the case of labeling) and indirectly (in the case of advertising) regulated by the FDA. The blanket speech ban here in issue, administered by the FDA, is substantively indistinguishable from the blanket bans imposed on these amici by FDA to prevent the communication of truthful dietary supplement health claims. *See Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999); *reh'g denied en banc*, 172 F.3d 72 (D.C.Cir. 1999)(hereinafter "*Pearson* I"); *Pearson v. Shalala*, 130 F. Supp.2d 105 (D.D.C. 2001) (hereinafter "*Pearson* II"); *Pearson v. Thompson*, 141 F. Supp.2d 105 (D.D.C. 2001) (hereinafter "*Pearson* III") (declaring such bans unconstitutional under the First Amendment). The legal validity of FDA blanket speech bans will likely be affected by this Court's First Amendment determination on the blanket ban here in issue. These amici thus have a keen interest in the outcome of the case.

SUMMARY OF ARGUMENT

Upholding the decision below protects the First Amendment presumption favoring disclosure of truthful, nonmisleading health information over its suppression. It reaffirms the principles first articulated in *Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council*, 425 U.S. 748 (1976), that weigh heavily against blanket bans on drug advertising.

In *Virginia State Board of Pharmacy* this Court held drug price information protected from a blanket advertising ban, reasoning that communication on the availability of the X prescription drug at the Y price was indispensable to consumers (indeed, was potentially more important to them than the day's most urgent political debate). *Id.* at 763. Here again the Court confronts a blanket ban on drug

advertising. That ban deprives physicians, including those among the amici, of information they need to locate competitively priced compounded drugs efficiently.

Drug compounding (the state regulated and licensed practice of manipulating drug content, delivery method, and dose to treat special needs patients) occurs on a case by case basis and is performed under state law either by individual physicians directly or by pharmacists pursuant to an individual physician's prescription. By contrast, drug manufacturing (the federally regulated production of standardized and FDA pre-approved drugs) occurs in mass, pre-set quantities and delivery forms for distribution to licensed drug retailers and licensed practitioners nationwide. Drug compounding when performed under state law is thus part of a physician's practice of medicine, a practice heavily regulated by the states. When a drug is prescribed by physicians for an unapproved use (i.e., for a use not evaluated by the FDA for safety or efficacy)—a practice especially common among oncologists and pediatricians—or is manipulated by or at the behest of a physician to satisfy the treatment needs of a specific patient, that is a "practice of medicine" regulated by the states. The "practice of medicine" is expressly exempt from federal regulation under the Food Drug and Cosmetic Act (FDCA). *See* 21 U.S.C. § 360(g)(2) (exempting "practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, or compound, or process drugs or devices solely for use in the course of their professional practice" from the FDCA drug registration and inspection provisions); *see also* 21 U.S.C. § 374(a)(2)(A);(B); *Chaney v. Heckler*, 718 F.2d 1174, 1180 (D.C. Cir. 1983). The petitioners thus err when they argue to the Court that prior to the adoption of the FDA Modernization Act, Pub. L. No. 105-115, 111 Stat. 2296 (1997) (FDAMA), there existed no statutory basis for exempting compounded drugs from the FDCA's pre-market approval provisions.

But even were the drug pre-market approval provisions deemed applicable to patient specific compounded drugs (as the petitioners presume they are), it is not true that the FDA, pre-FDAMA, deemed itself incapable of regulating interstate traffic in compounded drugs. To the contrary, FDA has previously assumed that the FDCA's drug manufacturing and distribution provisions, 21 U.S.C. § 351; 355 (2001), left unchallenged in this litigation, grant FDA authority to limit the amount of compounded drugs entering interstate commerce. FDA has also assumed that those sections of the FDCA grant it authority to limit the kinds of substances that may be shipped interstate for use in compounding. *See e.g.*, FDA, *Compliance Policy Guides* (hereinafter, "*CPG*") 7132.16 Chap. 4 § 460.200 (1992) (revoked by FDA following passage of FDAMA). Thus, without the FDAMA sections here in issue (and without need for resort to speech restrictions), the petitioners have limited the mass interstate distribution of compounded drugs and substances for use in compounded drugs.

To be sure, it is possible to limit the amount and kind of compounded drugs in interstate commerce without imposing a blanket ban on advertising of specific compounded drugs and drug prices. The petitioners presume, however, that the power to regulate commercial activity carries with it a "lesser" included power to regulate speech concerning that activity. That underlying premise of the petitioners' argument is substantively indistinguishable from a false syllogism rejected by this Court in 1996. The view that the power to regulate a commercial activity includes within it the power to regulate speech concerning that activity, the so-called "greater-includes-the-lesser" syllogism, is, post *44 Liquormart v. Rhode Island*, 517 U.S. 484, 510-513 (1996), not good law.

The petitioners insist that they must ban compounded drug advertising to protect patient health and safety, but that argument too is lacking in persuasive force because health and safety regulation of pharmacy and physician com-

pounding has long been a province of the states. For decades hospitals, physicians, and pharmacists have engaged in compounding under extensive state regulation. Contrary to the petitioners' argument, that state system has had an outstanding safety record. It has been patients' first line of protection since the advent of modern pharmacy compounding in the late 1960's. There is no basis, and certainly no record evidence, to question the adequacy or effectiveness of state health and safety regulation of pharmacy and physician compounding.

The Congress of the United States and the FDA have recognized that regulation of compounding, like regulation of medical and pharmacy practice, is a matter of state concern. The FDAMA exemption afforded compounded drugs from the new drug approval provisions of the FDCA is but one of several statutory and regulatory exceptions to the general rule requiring federal pre-market drug approval. Those exceptions (such as for the practice of medicine and pharmacy, including compounding; for unapproved uses of FDA approved drugs; for personal use importation of unapproved drugs from outside the United States; and for experimental use of unapproved drugs) provide physicians the flexibility they must have to treat patients for whom approved drugs are either inappropriate, ineffective, or dangerous.

Here, as in *Rubin v. Coors Brewing Company*, 514 U.S. 476 (1995), the Government's justification for its speech ban rests on an irrational regulatory scheme. On the one hand, the Government permits pharmacy advertising of the existence of compounding services, arguing that it can allow that advertising without fear of increased demand for compounded drugs. On the other, the Government forbids pharmacy advertising of the existence of specific compounded drugs at specific prices, arguing that it cannot allow that advertising without fear of increased demand for compounded drugs. The argument apparently presumes that physicians seeking compounded drugs will be less apt to find

those drugs if they are only informed of the places that sell them rather than of the availability, classes, types, and prices of compounded drugs sold. That argument is counterintuitive and wholly speculative backed by not one shred of record evidence despite its illogic. This Court has repeatedly rejected such speculative argument as insufficient to satisfy the Government's high First Amendment burden. *See Coors*, 514 U.S. at 487-489; *Edenfield v. Fane*, 507 U.S. 761, 770-771 (1993); *Ibanez v. Florida Department of Business and Professional Regulation*, 521 U.S. 136, 143 (1994); *Zauderer v. Office of Disciplinary Counsel of Supreme Court of Ohio*, 471 U.S. 626, 648-649 (1985). Logically, while less information may make the cost of obtaining a compounded drug higher than would otherwise be the case, it will likely not dissuade a physician intent on obtaining a compounded drug for a patient in need if that physician receives information on the existence and location of compounding pharmacies. Thus, the Government's position, dependent on speech suppression, provides at best only remote, indirect, and ineffective support, if any, for the Government's goal of keeping the demand for compounded drugs at some unarticulated lower than free market level.

In the present case the petitioners have not established that the FDAMA speech ban on compounded drug advertising (reaching even the phrase, "I will sell you the X compounded prescription drug at the Y price") directly and materially advances their goal of reducing to some unspecified below market level the amount of compounded drugs. They have not established the rationality of a regulatory scheme that allows advertising of compounding services but not of specific compounded drugs. They have not established the absence of numerous and obvious less restrictive alternatives (such as limits on the drugs available for compounding and on the amount of compounded drugs distributed interstate). Thus, having failed the direct advancement and means-ends tailoring prongs of *Central Hudson Gas & Electric v. Public*

Service Commission of New York, 447 U.S. 557 (1980) (as modified by its progeny), the Government's speech ban is unconstitutional. This Court should therefore uphold the decision of the United States Court of Appeals for the Ninth Circuit invalidating the speech ban.

This case is not unique. The lower federal courts have repeatedly condemned FDA blanket speech bans on truthful health information to no avail; FDA's acts of suppression continue largely unabated. *See Pearson I*, 164 F.3d 650; *Pearson II*, 130 F. Supp.2d 105; *Pearson III*, 141 F. Supp.2d 105; *see also* S.Rep. No. 105-43, at 50 (1997). The FDAMA blanket ban is thus part of a common, redundant approach favored by petitioners, an approach they employ undeterred by constitutional mandates in specific cases to the contrary. The precedential import and impact of the present case is thus profound and will necessarily be viewed as expressing the Court's willingness to condone similar FDA violations in future. The amici therefore urge the Court when resolving the current controversy to make clear that would-be health information speech police must abide by the same high First Amendment standard this Court expects of other would-be regulators of commercial speech, emphasizing that FDA regulators cannot shirk their constitutional duty to satisfy the First Amendment standard and must, consistent with that standard, favor disclosure of health information as the rule (relegating suppression to the status of a rare exception).

ARGUMENT

I. HEALTH AND SAFETY REGULATION OF COMPOUNDING HAS LONG BEEN A STATE PROVINCE

The preparation of patient-specific formulations by pharmacies and physicians (compounding [2]) has been a part of

---

[2] Compounding has been succinctly defined as a process by which a pharmacist "combines, mixes, or alters ingredients to create a certain

medical and pharmacy practice for thousands of years. In modern times, compounded preparations are essential for special needs patients, such as children and the elderly who may have difficulty swallowing patented drugs in their commercially available dosage forms; hospitalized patients who need parenteral nutrition for extended recuperative stays; and cancer patients who need compounded chemotherapy cocktails. It is thus no exaggeration to say that longevity and pain relief are in no small measure due to the ability of physicians, pharmacists, and veterinarians to compound medications expeditiously for their special needs patients.

A. The Historic and Indispensable Role of Compounding

Compounding is a practice as old as the first preparers of remedies for the first recorded civilizations.[3] Ancient Babylonian-Assyrian medicine included a class of "preparers of remedies" whose functions included compounding.[4] Compounding was practiced by apothecaries in ancient Egypt as recorded in the Ebers Papyrus circa 1500 B.C.[5] The scriptures refer to the art of the apothecary and to compounding: "And thou shalt make it an oil of holy ointment, an ointment compound after the art of the apothecary: It shall be an holy anointing oil." Exodus 30:25. *See also* Loyd V. Allen, Jr., Ph.D., *The Art, Science, and Technology of Pharmaceutical Compounding* xi (1998).

---

medication for a patient." *Professionals & Patients for Customized Care v. Shalala*, 847 F. Supp. 1359, 1361 (S.D. Tex. 1994), *aff'd*, 56 F.3d 592 (5th Cir. 1995).

[3] Loyd V. Allen, Jr., Ph.D., *The Art, Science, and Technology of Pharmaceutical Compounding* xi (1998)

[4] Edward Kremers and George Urdang, *History of Pharmacy: A Guide and a Survey* 4-7 (1947).

[5] *See id.* at 387; *see also* Charles H. LaWall, *The Curious Lore of Drugs and Medicines* 11 (1927).

During the Norman period in England, the word "apothecary . . . designated anyone who kept a shop or store of such nonperishable commodities as spices, drugs, combits, and preserves." Harold B. Gill, Jr., *The Apothecary in Colonial Virginia* 1 (1972). From approximately 1300 to 1500, "the term [apothecary] was restricted to those who prepared and sold drugs," *Id.* at 1.[6] Until the late 1700's apothecaries who learned their skills through apprenticeship performed roles commonly associated with physicians. *See id.* On the eve of the nineteenth century, there first arose a professional distinction between druggists and apothecaries, on the one hand, and physicians, on the other. *See id.* Before that time, it was common for apothecaries to diagnose disease and dispense drugs. *See id.* at 8.

In June 1632, Parliament passed a law making it unlawful for apothecaries to sell drugs without a physician's prescription, but the law was honored more in the breach. *See id.* Parliament's passage of the Apothecaries' Act of 1815 caused a true separation between the medical and pharmaceutical professions in England. *See id.* at 15. From the 17th century until at least 1851, apothecaries in America performed the dual role of druggist and physician.[7] Modern

---

[6] Even at this early date, concern arose among professionals for quality apothecaries and drugs, as evidenced by the words of English physician William Bulleyn who died in 1576:

> His place of dwelling must be cleanly, to please the senses withal. His garden must be at hand with plenty of herbes, seeds, and roots. He must have his mortars, stills, pots, filters, glasses, boxes, clean and sweete. He must have two places in his shop, one must be clean for physic, and [the other a] base place for chirurgic stuff. He is neither to [increase nor] diminish the physician's prescriptions. He is neither to buy nor sell rotten drugs . . . .

Id. at 14.

[7] During his 1788 travels in America, Frenchman Jacques P. Brissot de Warville observed: "The greatest part of these physicians [at Philadelphia] are, at the same time, apothecaries. They continue to unite these two

professional pharmacies first appeared in the United States in 1851.[8] It was not until the second World War, however, that consumers came to rely primarily on physicians, rather than apothecaries, for medical advice.[9] Moreover, patent medicines were quite scarce in America before the end of World War II. Consequently, local plants, such as Indian hemp, papoose root, Indian mallow, and snake root were commonly compounded by apothecaries. Gill, *supra*, at 40.

Modern regulation of pharmacy as a distinct profession began with model state laws initially introduced at the Chicago meeting of the American Pharmaceutical Association in 1869. *See* Kremers, *supra*, at 199. By 1909 all then extant states of the United States had adopted the model laws for the regulation of pharmacy. *See id.*

Despite the rise of mass manufactured drugs, compounding has remained an indispensable tool in modern medical and pharmaceutical practice.[10] In modern times, compounding permits physicians and veterinarians to respond to a wide variety of patient specific needs that cannot be accommodated, or cannot be accommodated adequately, with mass

---

sciences out of respect to the people, who wish that the man who orders the medicine should likewise prepare it." Gill, *supra*,. at 28.

[8] Kremers et al, *supra*, at 293.

[9] ". . .[A]t least until World War II, apothecaries, or druggists, were often the first to be called upon for medical advice." John Duffy, *From Humors to Medical Science: A History of American Medicine* 7-8 (1993). *See also* LaWall, *supra*, at 11.

[10] Loyd V. Allen, Jr., Ph.D. has explained the basic distinction between "manufacturing" and "compounding:" "In general, compounding differs from manufacturing in that compounding involves a specific practitioner-patient-pharmacist relationship, the preparation of a relatively small quantity of medication, and different conditions of sale (i.e., specific prescription orders)." *The Art, Science, and Technology of Pharmaceutical Compounding*, *supra*, at 1.

manufactured drugs.[11] Compounding occurs routinely in hospitals, physicians' offices, veterinary clinics, and pharmacies. In 1995, compounded prescriptions represented approximately 11% of all prescriptions dispensed.[12] Anyone hospitalized for more than a day is almost always the beneficial recipient of compounded drugs. "In hospitals, compounding has always been a part of pharmacy practice; intravenous admixture programs were brought into hospital pharmacy departments in the 1960s and 1970s and many pediatric formulations are prepared routinely." Loyd V. Allen, Jr., Ph.D., *Allen's Compounded Formulations: The U.S. Pharmacist Collection, 1995-1998* VII (1997). The ubiquitous "IV" is usually a compounded solution prepared to satisfy the particular needs of the hospitalized patient.

Examples of compounded products dispensed every day by health care professionals include total parenteral nutrition solutions; intrathecal solutions for pain management (such as morphine solutions); most intravenous admixtures; many antibiotic preparations for ambulatory care; and most oncology preparations. *See generally*, *Compounding Parenteral Nutrition Solutions*, 2 International Journal of Pharmaceutical Compounding 5 (1998); *Compounding for Pain Management*, 2 International Journal of Pharmaceutical Compounding 2 (1998); *Compounding for Pain Management*, 4 International Journal of Pharmaceutical Compounding 1 (2000); *Compounding for a Diverse Ambulatory Patient Base*, 1 International Journal of Pharmaceutical Compounding 6 (1997); *Compounding for Hospice and Cancer Patients*,

---

[11] *See The Art, Science, and Technology of Pharmaceutical Compounding*, *supra*, at 1: "Compounding is . . . essential to the provision of health care. Compounding can be as simple as the addition of a liquid to a manufactured drug powder, or as complex as the preparation of a multicomponent parenteral nutrition solution."

[12] *The Art, Science, and Technology of Pharmaceutical Compounding*, *supra*, at xii.

4 International Journal of Pharmaceutical Compounding 4 (2000). Pediatric medications are not generally available in an easy-to-swallow form; consequently pharmacists frequently make liquids for oral consumption from commercially available tablets/capsules. *See generally, Compounding for Pediatric Patients*, 5 International Journal of Pharmaceutical Compounding 1 (2001). Because those drugs often have relatively short shelf lives when put into solution, they must be compounded by the pharmacist. Geriatric medications for the elderly who have difficulty swallowing are also frequently compounded. *See generally, Exploring Compounding Options for Geriatric Patients*, 1 International Journal of Pharmaceutical Compounding 3 (1997). The need to vary dosage forms and to eliminate preservatives or allergy-producing excipients may lead a physician or pharmacist to cause a pharmaceutical product to undergo compounding before it is ingested or administered to a patient.[13]

Through compounding, pharmacists, physicians, and veterinarians prepare solutions, suspensions, topicals, and suppositories that provide alternative routes of administration sometimes necessary in the treatment of particular patients. They are also able to prepare select dosage forms from bulk drug ingredients. Compounding is required to prepare radioactive isotopes and cassettes, syringes, and other devices for drug administration in the home setting. *See id.* at xv-xvi.

There is now near universal scientific recognition of the need for compounding in the provision of patient care. In

[13] *See The Art, Science, and Technology of Pharmaceutical Compounding, supra*, at xii: "Complete pharmaceutical care must involve the dosage form, which might necessitate compounding a patient-specific form not available commercially; possibly the preparation of a product without a preservative or a specific allergy-producing excipient that must be removed from the formulation."

1990, the U.S. Pharmacopoeial Convention appointed a Pharmacy Compounding Practices Expert Advisory Panel to prepare a chapter on compounding for the USP and to prepare monographs on compounded products. The chapter on "Pharmacy Compounding Practices" appeared in 1996 and the first compounding monographs appeared in 1998. *See, Allen's Compounded Formulations, supra*, at 2; *see generally* United States Pharmacopoeial Convention, Inc., *United States Pharmacopoeia XXV/ National Formulary XX* (2002).

Far from constituting a health threat, compounding under state regulation is an indispensable tool in the treatment of disease and the alleviation of pain. Its modern use is a professional practice under the ever-watchful eye of state boards of medicine and pharmacy.[14]

B. Modern State Regulation of Compounding

Every state extensively regulates pharmacy practice, including compounding.[15] Compounding is not regulated

[14] In its first decision concerning price advertising by pharmacists, this Court recognized the high degree of professionalism associated with a state licensed pharmacy practice, writing:

> [T]he practice is subject to extensive regulation aimed at preserving high professional standards. . . . . The Board is broadly charged by statute with various responsibilities, including the "[m]aintenance of the quality, quantity, integrity, safety and efficacy of drugs or devices distributed, dispensed or administered." . . . It also is to concern itself with "[ma]intaining the integrity of, and public confidence in, the profession and improving the delivery of quality pharmaceutical services to the citizens of Virginia."

Virginia State Board of Pharmacy, 425 U.S. at 750-751.

[15] *See* Ala. Code § 34-23-1 *et seq.* (2001); Alaska Stat. § 08.80.003 *et seq.* (2001); Ariz. Rev. Stat. § 32-1901 *et seq.* (2001); Ark. code ann. § 17-92-101 *et seq.* (2001); Cal. Business and Professions Code § 4000 *et seq.* (West 2001); Colo. Rev. Stat. Ann. § 12-22-101 *et seq.* (West 2001); Conn. Gen. Stat. Ann. § 20-570 *et seq.* (West 2001); Del. Code Ann. tit. 24 § 2501 *et seq.* (2001); D.C. Code Ann. § 3-1201.01 *et seq.* (2001); Fla. Stat. ch. 465.001 *et seq.* (2001); Ga. Code Ann. § 26-4-1 *et seq.* (2001);

separate from pharmacy but is accepted as an integral part of it. Consider, for example, Maryland's rather typical statutory definition of pharmacy practice:

> [To] "practice pharmacy" means to engage in any of the following activities:
>
> (i) Providing pharmaceutical care;
>
> (ii) Compounding, dispensing, or distributing prescription drugs or devices;
>
> (iii) Compounding or dispensing nonprescription drugs or devices;
>
> (iv) Monitoring prescriptions for prescription and nonprescription drugs or devices;

Haw. Rev. Stat. Ann. § 461-1 *et seq.* (2001); Idaho Code § 54-1701 *et seq.* (2001); 225 Ill. Comp. Stat. Ann. 85/1 *et seq.* (West 2001); Ind. Code. Ann. § 25-26-13-1 *et seq.* (2001); Iowa Code Ann. § 155A.1 *et seq.* (West 2001); Kan. Stat. Ann. § 1625 *et seq.* (2000); Ky. Rev. Stat. Ann. § 315.002 *et seq.* (Michie 2001); La. Rev. Stat. Ann. § 1161 *et seq.* (West 2001); Me. Rev. Stat. Ann. tit. 32, § 13701 *et seq.* (West 2000); Md. Code Ann. Health Occupations § 12-101 *et seq.* (2001); Mass. Gen. Laws Ann. 112 § 24 *et seq.* (2001); Mich. Comp. Laws § 333.17701 *et seq.* (2001); Minn. Stat. § 151.01 *et seq.* (2001); Miss. Code Ann. § 73-21-69 *et seq.* (2001); Mo. Ann. Stat. § 338.010 *et seq.* (West 2001); Mont. Code Ann. § 37-7-101 *et seq.* (2001); Neb. Rev. Stat. § 71-1,142 *et seq.* (2001); Nev. Rev. Stat. Ann. § 639.001 *et seq.* (2001); N.H. Rev. Stat. Ann. § 318:1 *et seq.* (2001); N.J. Stat. Ann. § 45:14-11:11 *et seq.* (2001); N.M. Stat. Ann. § 61-11-2 *et seq.* (Michie 2001); N.Y. Educ. Law § 6800 *et seq.* (2001); N.C. Gen. stat. § 90-85.2 *et seq.* (2000); N.D. Cent. Code § 43-15-01 *et seq.* (2001); Ohio Rev. Code Ann. § 4729.01 *et seq.* (Anderson 2000); Okla. Stat. tit. 59, § 353 *et seq.* (2000); Or. Rev. Stat. § 689.005 *et seq.* (2000); Pa. Stat. Ann. tit. 63, § 390-1 *et seq.* (West 2001); R.I. Gen. Laws § 5-19-1 *et seq.* (2001); S.C. Code Ann. § 40-43-10 *et seq.* (West 2000); S.D. Codified Laws § 36-11-1 (Michie 2001); Tenn. Code Ann. § 63-10-301 *et seq.* (2001); Tex. Occ. Code Ann. § 551.001 *et seq.* (West 2001); Utah Code Ann. § 58-17a-101 *et seq.* (2001); Vt. Stat. Ann. tit. 26 § 2021 *et seq.* (2001); Va. Code Ann. § 54.1-3300 (Michie 2001); Wash. Rev. Code Ann. § 18.64.001 *et seq.* (2001); W. Va. Code § 30-5-1 *et seq.* (2001); Wis. Stat. Ann. § 450.01 *et seq.* (West 2001); Wyo. Stat. Ann. § 33-24-101 *et seq.* (2001).

> (v) Providing information, explanation, or recommendations to patients and health care practitioners about the safe and effective use of prescription or nonprescription drugs or devices; or
>
> (vi) Identifying and appraising problems concerning the use or monitoring of therapy with drugs or devices.

Md. Code Ann. Health Occupations § 12-101.

Pharmacists and physicians who compound and physicians who prescribe compounded drugs must adhere to generally recognized standards of care enforced by state boards of pharmacy and medicine.[16]

---

[16] *See* (Pharmacists) Ala. Code § 34-23-2; Alaska Stat. §§ 08.80.003-08.80.005; Ariz. Rev. Stat. § 32-1904; Ark. code ann. § 17-92-205(a); Cal. Business and Professions Code § 4005; Colo. Rev. Stat. Ann. § 12-22-101; Conn. Gen. Stat. Ann. § 20-576; Del. Code Ann. tit. 24 § 2501; D.C. Code Ann. § 3-1204.08; Fla. Stat. ch. 465.002; Ga. Code Ann. § 26-4-3; Haw. Rev. Stat. Ann. § 461-1; Idaho Code § 54-1702; 225 Ill. Comp. Stat. Ann. 85/1; Ind. Code. Ann. § 25-26-13-1; Iowa Code Ann. § 155A.2; Kan. Stat. Ann. § 65-1627; Ky. Rev. Stat. Ann. § 315.002; La. Rev. Stat. Ann. § 1162; Me. Rev. Stat. Ann. tit. 32, §§ 13711, 13721, 13723; Md. Code Ann. Health Occupations § 12-205; Mass. Gen. Laws Ann. 112 § 24; Mich. Comp. Laws § 333.17722; Minn. Stat. § 151.01; Miss. Code Ann. § 73-21-83; Mo. Ann. Stat. § 338.140; Mont. Code Ann. §§ 37-7-101, 37-7-201; Neb. Rev. Stat. § 71-1,142.09; Nev. Rev. Stat. Ann. § 639.070; N.H. Rev. Stat. Ann. § 318:5-a; N.J. Stat. Ann. § 45:14-14:1,45:14-3; N.M. Stat. Ann. § 61-11-6; N.Y. Educ. Law § 6804; N.C. Gen. stat. §§ 90-85.2, 90-85.6; N.D. Cent. Code § 43-15-10; Ohio Rev. Code Ann. §§ 4729.02, 4729.04; Okla. Stat. tit. 59, §§ 353, 353.7; Or. Rev. Stat. §§ 689.025, 689.135; Pa. Stat. Ann. tit. 63, § 390-6; R.I. Gen. Laws § 5-19-6; S.C. Code Ann. § 40-43-60; S.D. Codified Laws §§ 36-11-1, 36-11-11; Tenn. Code Ann. § 63-10-501; Tex. Occ. Code Ann. § 554.002; Utah Code Ann. § 58-17a-201; Vt. Stat. Ann. tit. 26 § 2032; Va. Code Ann. § 54.1-3305; Wash. Rev. Code Ann. § 18.64.005; W. Va. Code § 30-5-2; Wis. Stat. Ann. § 450.02; Wyo. Stat. Ann. § 33-24-102. *See also* (Physicians) Ala. Code § 34-24-53; Alaska Stat. §§ 08.64.100, 08.64.101; Ariz. Rev. Stat. § 32-1403; Ark. code ann. § 17-95-303; Cal. Business and Professions Code § 2220; Colo. Rev. Stat.

II. CONGRESSIONAL AND FDA RECOGNITION AND ACCEPTANCE OF STATE COMPOUNDING REGULATION

Almost sixty years before adoption of FDAMA, Congress chose to exempt from FDA drug registration and inspection pharmacies and physicians whose compounding practices complied with state laws governing those practices.[17] Congress also chose to exempt from FDCA misbranding provisions any drug dispensed by filling or refilling a valid prescription from a licensed physician.[18]

Before FDAMA, federal courts understood 21 U.S.C. § 360(g)(2) to create a "practice of medicine" exemption to the FDCA. *See Cowan v. United States,* 5 F. Supp.2d 1235,

---

Ann. §§ 12-36-102, 12-36-104; Conn. Gen. Stat. Ann. § 20-8a; Del. Code Ann. tit. 24 §§ 1701, 1730; D.C. Code Ann. § 3-1202.03, 3-1204.08; Fla. Stat. ch. 458.307; Ga. Code Ann. § 43-34-21; Haw. Rev. Stat. Ann. § 453-5.1; Idaho Code § 54-1806; 225 Ill. Comp. Stat. Ann. §§ 60/8, 60/9; Ind. Code. Ann. § 25-22.5-2-7; Iowa Code Ann. § 148.2A; Kan. Stat. Ann. § 65-2812; Ky. Rev. Stat. Ann. § 311.565; La. Rev. Stat. Ann. § 1261; Me. Rev. Stat. Ann. tit. 32, § 3269; Md. Code Ann. Health Occupations § 12-101; Mass. Gen. Laws Ann. 112 § 2; Mich. Comp. Laws § 333.17021; Minn. Stat. § 147.001; Miss. Code Ann. §§ 73-25-3, 73-25-30; Mo. Ann. Stat. § 334.120; Mont. Code Ann. §§ 37-3-203, 37-3-101; Neb. Rev. Stat. § 71-111,71-1,104.06; Nev. Rev. Stat. Ann. §§ 630.003, 630.130; N.H. Rev. Stat. Ann. § 329:2; N.J. Stat. Ann. §§ 45:9-22.1, 45:9-22:18; N.M. Stat. Ann. §§ 61-6-10.8, 61-6-10.9; N.Y. Educ. Law §§ 6508, 6509; N.C. Gen. stat. § 90-2; N.D. Cent. Code § 43-17-07.1; Ohio Rev. Code Ann. § 4731.20; Okla. Stat. tit. 59, §§ 481, 509; Or. Rev. Stat. §§ 677.015, 677.265; Pa. Stat. Ann. tit. 63, §§ 422.3, 422.8; R.I. Gen. Laws § 5-37-1.3; S.C. Code Ann. § 40-47-20; S.D. Codified Laws § 36-4-29; Tenn. Code Ann. § 63-6-101; Tex. Occ. Code Ann. § 153.001; Utah Code Ann. § 58-67-201; Vt. Stat. Ann. tit. 26 § 1353; Va. Code Ann. § 54.1-2911; Wash. Rev. Code Ann. § 18.71.015; W. Va. Code §§ 30-3-1, 30-3-7; Wis. Stat. Ann. § 448.02; Wyo. Stat. Ann. § 33-26-202.

[17] 21 U.S.C. §§ 360(g)(1);(2); 374(a)(2)(A);(B).

[18] 21 U.S.C. § 353(b)(2).

1240-1241 (N.D. Okla. 1998); *United States v. Algon Chemical, Inc.*, 879 F.2d 1154 (3rd Cir. 1989); *Chaney,* 718 F.2d 1174. In *Chaney*, the D.C. Circuit explained the purpose of the exemption as follows:

> The better explanation for the practice-of-medicine exemption is that Congress did not want to interfere with physicians' treatment of their patients. New uses for drugs are often discovered after FDA approves the package inserts that explain a drug's approved uses. Congress would have created havoc in the practice of medicine had it required physicians to follow the expensive and time-consuming procedure of obtaining FDA approval before putting drugs to new uses. Thus Congress exempted the practice of medicine from the Act so as not to limit a physician's ability to treat his patients.

718 F.2d at 1180.

Prior to FDAMA, FDA had generally exercised enforcement discretion to avoid the prosecution of physicians and pharmacists whose compounding practices with unapproved drug substances did not introduce into interstate commerce harmful drug products. *See e.g., CPG* 7132.16. FDA did so recognizing that drug compounding, as opposed to drug manufacturing, was a legitimate practice when performed by licensed professionals under state law. In 1992 FDA adopted its *CPG* 7132.16 (rescinded in January of 1999 to implement the compounding provisions of FDAMA (*see* 64 Fed. Reg.1,207)). Another FDA *CPG* allows within certain limits the compounding of veterinary drugs. *See CPG* 7125.40 Chap. 6 § 608.400 (2001).

III. COMPOUNDING IS BUT ONE OF SEVERAL EXEMPTIONS FROM THE FDCA'S DRUG APPROVAL PROCESS

The "practice-of-medicine" exemption, 21 U.S.C. § 360(g)(2) (exempting "practitioners licensed to prescribe or administer

drugs or devices and who manufacture, prepare, propagate, compound, or process drugs or devices" from the FDCA's registration and inspection requirements) (see also 21 U.S.C. § 374(a)(2)(A);(B)), like the FDAMA exemptions for pharmacy compounding, are not unique. By FDA policy, under certain circumstances unapproved drugs may be imported into the United States on the prescription of a physician. *See* FDA, *Regulation Procedures Manual* (hereinafter "*RPM*"), "Coverage of Personal Importation," Chapter 9, (August 1997). Moreover, FDA has long allowed unapproved uses of approved drugs. *See* Stuart L. Nightingale, M.D., *Use of Drugs for Unlabeled Indications*, FDA Perspective, 269 (September 1986). Further, unapproved drugs may be prepared for and administered by physicians in clinical trials authorized by FDA. 21 U.S.C.A. § 355(I); 21 C.F.R. § 312 (2001). Those caveats to the general rule have also been crafted in recognition of the professional status of physicians and pharmacists and their independent regulation by the states.

A. The Statutory and Regulatory Exemptions from New Drug Approval

1. *Personal Use Importation of Unapproved Drugs*

While it is generally illegal to import unapproved drugs, in response to a market that demands medical treatments lawful abroad but not domestically FDA has created a personal use importation policy. That policy permits unapproved drugs to be imported via personal baggage or mail shipment into the United States in personal-use quantities. *See generally, RPM, supra*, at Chap. 9.

2. *Unapproved Uses of Approved Drugs*

Under 21 U.S.C. § 352, the FDA has no authority to regulate the practice of medicine or to restrict the manner in which a physician may use an FDA approved drug. Indeed,

Congress did not intend FDA to regulate the practice of medicine or to interfere with a physician's ability to treat patients. *See* S. Rep. No. 74-361, at 3 (1935); S. Rep. No. 74-646, at 1 (1935) (explaining that the enactment of the FDCA was not intended to permit FDA to interfere with medical practice as between the physician and patient); H.R. Rep. No. 74-2755, at 5 (1936); S.Rep. No. 87-1744, pt. 1; at 56 (1962). Case law also confirms that the FDCA does not grant FDA authority to prohibit a doctor from prescribing a lawful drug for a purpose not approved by FDA. *See Cowan*, 5 F. Supp. 2d at 1240-1241; *Algon Chemical*, 879 F. 2d at 1160-1163; *Chaney*, 718 F.2d at 1180, *rev'd on other grounds*, 470 U.S. 821(1985); *United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981).

Moreover, FDA recognizes that unapproved uses of approved drugs may be appropriate and necessary, and may even represent important therapeutic innovations by physicians. *See Use of Drugs for Unlabeled Indications*, *supra*, at 269; Stuart L. Nightingale, M.D., *Unlabeled Uses of Approved Drugs*, 26 Drug Information Journal 141 (1992). FDA recognizes that accepted medical practice can include a use for a drug that is not included in its approved uses and that the unapproved use may be appropriate if based on controlled clinical trials or reliable medical opinion. *See Unlabeled Uses of Approved Drugs*, *supra*, at 142, *citing* 37 Fed. Reg. 16,503 (1972). Prescriptions for unapproved uses are common among pediatricians and oncologists. *See* American Academy of Pediatrics, *Few Prescription Drugs Labeled for Pediatric Use*, ¶ 1, 3 (visited Dec. 20, 2001) <http://www.babybag.com/articles/aap_drug.htm>; Daniel Troy, *The FDA and Off-Label Uses of Drugs and Devices*, ¶ 3 (visited Dec. 20, 2001) <http://www.mediainst.org/ digest/97fall/wlf.html>.

3. *Investigational Use of Drugs*

By statute and regulation, it has long been lawful for qualified physicians to use unapproved new drugs in clinical trials authorized by FDA. *See* 21 U.S.C.A. § 355(I); 21 C.F.R. § 312.

B. FDA's Pre-FDAMA Limits on Substances Used in Compounding and on Interstate Distribution of Compounded Drugs

While the statutory exemption for the practice of medicine, 21 U.S.C. § 360(g)(2), would appear to entrust the states with the authority to regulate compounding, pre-FDAMA, FDA has construed its statutory authority to allow the imposition of federal limits on the amount of interstate distribution of compounded drugs and on the substances available for compounding. *See* 21 U.S.C. § 353 A(B)(1)(A). While the exercise of that pre-FDAMA authority is not before this Court, the petitioners lack credibility when they argue that they depend upon FDAMA's speech ban to limit the amount of compounded drugs in interstate commerce.

C. The Non-Speech Provisions of the FDCA, Left Unchallenged in This Litigation, Have Been Construed to Permit Regulation of the Amount of Compounding and, To a Large Extent, the Availability of Substances for Compounding

Prior to FDAMA FDA issued a Compliance Policy Guide ("CPG"), "Manufacture, Distribution, and Promotion of Adulterated, Misbranded, or Unapproved New Drugs for Human Use by State Licensed Pharmacies," reflecting long-standing FDA policy on drug compounding articulated in related compliance policy guides, warning letters, and federal court decisions. *See CPG* 7132.16 (rescinded when the FDAMA provisions on drug compounding became effective, 64 Fed. Reg. 1,207). Under the CPG, FDA threatened

enforcement action against any pharmacy that compounded "in inordinate amounts . . . drug products that [were] commercially available in the marketplace" or were "essentially generic copies of commercially available, FDA-approved drug[s]." Moreover, FDA threatened enforcement action against any pharmacy that received, stored, or used drug substances not made in "FDA approved facility[ies]" or that distributed "inordinate amounts of compounded products out of state." *See* CP6 7132.16. Thus, through pre-FDAMA enforcement policy, FDA construed its statutory authority as authorizing it to limit the amount and kind of compounded drugs prepared and distributed in interstate commerce.

IV. THE POWER TO REGULATE COMPOUNDING DOES NOT INCLUDE THE POWER TO REGULATE TRUTHFUL AND NONMISLEADING ADVERTISING

The petitioners' argument rests on an unmistakably clear premise that the power to regulate compounding, a commercial activity, includes within it the power to regulate advertising about that activity. In other words, the petitioners essentially reassert that the power to regulate a commercial activity is a power greater than that to regulate truthful and nonmisleading advertising about that activity. Yet that very "greater-includes-the-lesser" syllogism is a false one in our constitutional system. It guts the First Amendment presumption in favor of speech by rendering general regulatory power over commercial activity superior to constitutional protection for truthful speech. This Court has rejected the syllogism. *See, e.g., 44 Liquormart*, 517 U.S. at 510-513 ("Further consideration persuades us that the 'greater-includes-the-lesser' argument should be rejected for the . . . reason that it is inconsistent with both logic and well-settled doctrine"); *see also* Kurland, *Posadas de Puerto Rico v. Tourism Company: "'Twas Strange, 'Twas Passing Strange; 'Twas Pitiful, 'Twas Wondrous Pitiful,"* 1986 S.Ct.Rev. 1, 12-15.

Furthermore, the fact that in FDAMA the Government conditions receipt of a statutory exemption from the new drug approval requirements on relinquishment of the right to speak in no way lessens the First Amendment violation present. As the Court explained in *44 Liquormart*:

> Even though government is under no obligation to provide a person, or the public, a particular benefit, it does not follow that conferral of the benefit may be conditioned on the surrender of a constitutional right. *See, e.g., Frost & Frost Trucking Co. v. Railroad Comm'n of Cal.*, 271 U.S. 583, 594 (1926). In *Perry v. Sindermann*, 408 U.S. 593 (1972), relying on a host of cases applying that principle during the preceding quarter century, the Court explained that government "may not deny a benefit to a person on a basis that infringes his constitutionally protected interests—especially his interest in freedom of speech." *Id.*, at 597. That teaching clearly applies to state attempts to regulate commercial speech, as our cases striking down bans on truthful, nonmisleading speech by licensed professionals attest. *See, e.g., Bates v. State Bar of Ariz.*, 433 U.S. at 355; *Virginia Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976).

Id. at 513.

It is thus the case that the Government cannot overcome the strong First Amendment presumption in favor of truthful and nonmisleading commercial speech on the basis that its speech ban is limited to those who seek to engage in a commercial activity that it could lawfully limit.

Could it be that truthful compounded drug advertising is less deserving of First Amendment protection than other commercial speech? If there was any doubt about the intrinsic First Amendment value of truthful drug advertising, that doubt should have been put to rest in *Virginia State Board of Pharmacy,* 425 U.S. 748. The advertising ban at issue in *Virginia State Board* is in no respect materially

different from the advertising ban at issue here. Both forbid drug advertising, including communication of the following: "I will sell you the X prescription drug at the Y price." The *Virginia State Board* decision includes recognition that drug advertising carries with it profound importance for the price conscious consumer. That consumer could be a patient, as in *Virginia State Board*, or, as here, a physician searching for competitively priced compounded drugs for his special needs patient(s). The Court explained that drug advertising includes information essential for "the alleviation of physical pain or the enjoyment of basic necessities." *Id.* at 763-764. The free flow of that information is indispensable to the efficient and effective rendering of numerous private economic decisions whether made by patients directly or by physicians who must purchase compounded drugs expeditiously. *See id.* at 765. As in *Virginia State Board*, so too here, the advertising ban "does not directly affect" the alleged government interest "one way or the other." *Id.* at 769. Rather, "it affects" those interests "only through the reactions it is assumed people will have to the free flow of drug price information." *Id.* Yet, as this Court has stated repeatedly, governmental assumptions are not enough to overcome the First Amendment presumption in favor of disclosure over suppression. Indeed, the First Amendment has made disclosure the rule and suppression the exception, limited to circumstances of compelling justification, not to ones involving sheer speculation as to market reaction. *See* id at 770.

V. THE GOVERNMENT'S JUSTIFICATION FOR BANNING ADVERTISING OF SPECIFIC COMPOUNDED DRUGS AND PRICES, BUT NOT OF THE AVAILABILITY OF COMPOUNDING SERVICES, LACKS RATIONALITY AND FAILS THE DIRECT AND MATERIAL ADVANCEMENT TEST

The petitioners argue that they must prohibit the advertising of specific compounded drugs and prices to encourage a reduction in the amount of compounded drugs and thereby reduce the risk that pharmacies will overstep a line they leave undefined between permitted "compounding" and prohibited "manufacturing." Nevertheless, the petitioners do allow advertising of the availability of compounding services by pharmacists.

The Government's position is self-defeating and irrational. It rests on the counterintuitive assumption that physicians intent on compounding will be dissuaded from doing so if their contacts with compounding pharmacies are based on general advertisements of the availability of pharmacy compounding services rather than on specific advertisements of the availability and price of pharmacy compounded drugs. In short, the Government asks the Court to accept on faith that allowance of the one kind of advertising and disallowance of the other will result in a reduction in overall compounding activity such that the undefined and thus elusive point at which drug "manufacturing" takes place will not be reached. But the Government's scheme is wholly illogical. Backed by nothing but counterintuitive supposition, it is irrational and, thus, incapable of justifying a blanket speech ban.

The Court rejected a similar irrational scheme in *Coors*, 514 U.S. 476. In *Coors*, the Government argued that a statutory prohibition on placement of alcohol content on beer labels and in beer advertising lessened "strength wars" by

reducing competition among brands based on the potency of beer. But the law in question allowed alcohol content labeling in states that required such labeling and limited its ban on alcohol content advertising to those states that affirmatively prohibited such advertising. The regulatory scheme thus failed to advance directly and materially the Government's interest due to the "overall irrationality of the Government's regulatory scheme." *Coors*, 514 U.S. at 488.

Likewise, here, if the Government's true aim is to prevent compounding from becoming "drug manufacturing," it makes no rational sense to prohibit pharmacies from advertising specific compounded drugs and prices but permit them to advertise the availability of compounding services. The regulatory scheme is self-defeating and irrational. Like the scheme in *Coors*, the one here cannot directly and materially advance the Government's asserted interest.

VI. THERE ARE NUMEROUS AND OBVIOUS LESS RESTRICTIVE NON-SPEECH REGULATORY ALTERNATIVES TO THE GOVERNMENT'S SPEECH BAN

The petitioners lack credibility when they argue they need the FDAMA provisions stricken by the Ninth Circuit to reduce the amount of compounding to some unidentified below market level when prior to FDAMA FDA assumed power to limit the amount of compounded drugs in interstate commerce (and the substances available for compounding) based on its interpretation of the unamended FDCA. *See CPG* 7132.16. It is of course within the power of Congress to enact statutory provisions that limit the amount of compounded drugs in interstate commerce or that grant FDA authority to identify substances that may not be used in compounding, all without resort to a blanket ban on compounded drug advertising. Furthermore, the Government's concern that physicians may regard compounded drugs as

FDA approved if advertising is permitted can be resolved in the first instance by mandating use of a reasonable disclaimer to that effect. This Court has repeatedly held use of reasonable disclaimers constitutionally preferable to outright speech suppression. *See 44 Liquormart*, 517 U.S. at 499-500; *Ibanez*, 512 U.S. at 144-46; *Peel v. Attorney Registration & Disciplinary Comm'n of Illinois*, 496 U.S. 91, 110 (1990); *In re RMJ*, 455 U.S. 191, 203 (1982); *Central Hudson*, 447 U.S. at 571; *Bates*, 433 U.S. at 383-384. The lower courts have repeatedly ordered FDA to accept disclaimers as a less restrictive alternative to outright suppression of vital health information. *See Pearson* I, 164 F.3d 650; *Pearson* II, 130 F. Supp.2d 105; *Pearson* III, 141 F. Supp.2d 105; *see also Washington Legal Foundation v. Henney*, 56 F. Supp.2d 81, 87 (D.D.C. 1999) *rev'd on other grounds* 202 F.3d 331 (D.C.Cir. 2000). Finally, it is indeed true (albeit effectuation of this option would be harmful to Americans) that Congress could prohibit compounding altogether, again without violating the First Amendment (unless it could be shown that congressional action was motivated by a desire to suppress protected speech). The Court has regularly accepted the existence of numerous and obvious less restrictive alternatives to speech bans as evidence of an inadequate fit between the regulatory means chosen and the ends. That inadequate fit warrants invalidation of the FDAMA speech ban under the final prong of the *Central Hudson* test. *See Central Hudson*, 447 U.S. at 566; *see also 44 Liquormart*, 517 U.S. at 507-508; *Ibanez*, 512 U.S. at 143; *Edenfield*, 507 U.S. at 771-772.

VII. SEVERAL LOWER FEDERAL COURT CASES REVEAL THE FDAMA SPEECH BAN TO BE PART OF A GENERAL FDA PATTERN OF SPEECH SUPPRESSIVE ACTIONS, ALL DIRECTLY INFLUENCED BY THE COURT'S RESOLUTION OF THE FIRST AMENDMENT ISSUE IN THIS CASE

The published cases in the lower federal courts concerning FDA regulation of speech reveal that the agency has repeatedly relied on blanket speech bans and has refused to abide by the requirements of the First Amendment. *See Pearson* I, 164 F.3d 650; *Pearson* II, 130 F. Supp.2d 105; *Pearson* III, 141 F. Supp.2d 105; *Washington Legal Foundation*, 56 F. Supp.2d 81. Indeed, the amici here include plaintiffs in litigation against the agency in three of those four First Amendment cases. Repeatedly, those decisions have faulted the FDA for suppressing vital health information on labels and in labeling. In one such case, the FDA suppressed a folic acid/neural tube defect claim that daily consumption of folic acid by women of childbearing age could reduce the incidence of neural tube defect births and deaths by as much as 50 percent. Congress found FDA's suppression of that claim contributed to many preventable neural tube defects. *See* S.Rep. No. 105-43, at 50 (1997) ("Undoubtedly, many children suffered from preventable neural tube defects as a result of FDA's delay in authorizing health claims"). Thus, there is an urgent need for this Court to make clear once again that adherence to the First Amendment is imperative and that neither Congress nor the FDA enjoy an exception from the Constitution's strictures when either presumes to regulate the communication of health information.

CONCLUSION

For the foregoing reasons, the decision of the United States Court of Appeals for the Ninth Circuit should be affirmed.

Respectfully submitted,

JONATHAN W. EMORD *
CLAUDIA A. LEWIS-ENG
ANDREA G. FERRENZ
EMORD & ASSOCIATES, P.C.
5282 Lyngate Court
Burke, VA 22015
(202) 466-6937

* Counsel of Record

January 11, 2002

Attorney for Amici Curiae Dr. Julian M. Whitaker; Durk Pearson; Sandy Shaw; Pure Encapsulations, Inc.; American Association for Health Freedom; Wellness Lifestyles, Inc. d/b/a American Longevity; Hero Nutritionals, Inc.; Life Enhancement Products, Inc.; Life Extension Foundation; Life Services Supplements, Inc.

Supreme Court, U.S.
FILED
JAN 9 2002
CLERK

No. 01-344

IN THE

Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL.,

PETITIONERS,

v.

WESTERN STATES MEDICAL CENTER, *ET AL.*,

RESPONDENTS.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

BRIEF OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENTS

SUSAN C. WINCKLER
AMERICAN PHARMACEUTICAL ASSOCIATION
2215 CONSTITUTION AVENUE, NW
WASHINGTON, DC 20037

MICHAEL H. MCCONIHE
COUNSEL OF RECORD

KEVIN A. KERNAN
O'BRIEN, BUTLER, MCCONIHE & SCHAEFER, PLLC
888 17TH STREET, NW
SUITE 1000
WASHINGTON, DC 20006
(202) 298-6161

COUNSEL FOR AMICUS CURIAE AMERICAN PHARMACEUTICAL ASSOCIATION

Balmar Legal Publishing Services, Falls Church, VA (703) 289-9000

BEST AVAILABLE COPY

TABLE OF CONTENTS

TABLE OF AUTHORITIES ..... ii-iv

INTEREST OF AMICUS CURIAE 1

SUMMARY OF ARGUMENT 2

STATEMENT OF FACTUAL CONSIDERATIONS 4

I. The Practice of Pharmacy 4

II. Pharmacy Compounding 5

III. Types of Compounding 8

A. Compounding in Cancer Treatment 9

B. Compounding for Pediatric Patients 9

C. Compounding in Hospitals 9

D. Compounding in Hospice Care 10

IV. Preparation of Compounded Pharmaceuticals - Regulatory Changes 11

ARGUMENT 13

I. Compounding is not Manufacturing 13

II. A Compounded Drug Product is not a "New Drug" as Contemplated in FDCA and FDAMA 20

A. The Federal Food, Drug, and Cosmetic Act of 1938 21

B. The Food and Drug Administration Modernization Act of 1997 22

CONCLUSION 24

TABLE OF AUTHORITIES

Cases: **Page(s)**

Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837, 104 S.Ct. 2778 (1984)..... 19

Professionals and Patients for Customized Care v. Shalala, 847 F.Supp. 1359 (S.D. Tex. 1994).... 19

Professionals and Patients for Customized Care v. Shalala, 56 F.3d 592 (C.A.5 (Tex.) 1995)..... 19

United States v. Algon Chem., Inc., 879 F.2d 1154 (3rd Cir. 1989) 17, 18

United States v. Baxter Healthcare Corp., 901 F.2d 1401 (7th Cir. 1990)..... 18, 19

United States v. 9/1 Kg. Containers, 854 F.2d 173 (7th Cir. 1988)..... 17, 18

United States v. Sene X Eleemosynary Corp., 479 F.Supp. 970 (S.D. Fla. 1979)..... 19, 20

Statutes and Regulations

21 U.S.C. § 201 (p)(1) 3

21 U.S.C. § 201 (p)(2) 3

21 U.S.C. § 301 et seq. 2, 21

21 U.S.C. § 353a (Supp. V. 1999)..... 2, 3

21 U.S.C. § 353a (a) (Supp. V. 1999) 22, 24

21 U.S.C. § 353a (b)(1) (Supp. V. 1999)..... 23

21 U.S.C. § 353a (b)(1)(C) (Supp. V. 1999) 23

21 U.S.C. § 353a (b)(1)(D) (Supp. V. 1999)..... 22

21 U.S.C. § 353a (b)(3)(A) (Supp. V. 1999)..... 23, 24

21 U.S.C. § 353a (b)(3)(B) (Supp. V. 1999) 23

21 U.S.C. § 353a (c) (Supp. V. 1999) 24

21 U.S.C. § 355(a)..... 21

21 U.S.C. § 355(b)..... 3

21 U.S.C. § 355(d)..... 3

21 U.S.C. § 355(e)..... 3

21 U.S.C. § 360(g)(1) 3, 18, 19

21 U.S.C. § 360(g)(2) 18

21 U.S.C. § 374(a)(1) 18

21 U.S.C. § 374(a)(2)(A)..... 3, 18, 19

21 U.S.C. § 503a (a)(1)(A)..... 8

21 U.S.C. § 503a (a)(1)(B)..... 8

21 U.S.C. § 503a (a)(2)(A)..... 8, 16

21 U.S.C. § 503a (a)(2)(B) 8, 16

Alaska Stat. § 8.80.480 14..... 15

Ga. Code Ann. § 26-4-5(23)..... 15

La. Rev. Stat. Ann. § 1164 15

Miss. Code Ann. § 73-21-73(q)..... 15

N.H. Rev. Stat. Ann. § 318.1 (VIII) 15

N.M. Stat. Ann. § 61-11-2.Q. 15

Okla. Stat. tit. 59, § 353-1(20)..... 15

S.C. Code Ann. § 40-43-30(29)..... 15

Tenn. Code Ann. § 63-10-404(18) 15

W. Va. Code Ann. § 30-5-1b(o). 15

Miscellaneous:

Hospice Care and the Pharmacist, 1 International Journal of Pharmaceutical Compounding 11 (January/February 1997).....11

Knowlton, C.H., *J APhA 1997, NS 37 (3): 361*.....13

Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy, §§ 104 and 105(f) 12

NABPLAW ® Pharmacy law database, NABP's database of state pharmacy practice acts and regulations.....12

The National Association of Boards of Pharmacy Good Compounding Practices Applicable to State Licensed Pharmacies, Subpart A., Park Ridge, IL NABP, 1993 .....13, 14, 16

S. Rep. No. 105-43, 105th Cong. 1st Sess. 67-68 (1997).....17

Pharmacy Compounding Practice and Sterile Drug Products for Home Use, Rockville, Maryland: U.S. Pharmacopeia, 1996.....7, 8

Wooten, A.C., *Chronicles of Pharmacy, quoted in* Dinah G. Jordan, *Pharmacist Compounding v. Veterinarian Compounding: Similarities and Differences*, 205 JAVMA 256 (1994).....6

INTEREST OF AMICUS CURIAE [1]

The American Pharmaceutical Association ("APhA") is the national, professional society of pharmacists. It is a voluntary membership organization of over 50,000 individuals, including pharmacists, pharmaceutical scientists and pharmacy students. Its pharmacist members are engaged in virtually every area of pharmacy practice, including independent and chain community pharmacy practice, hospital pharmacy practice, nuclear pharmacy practice, long term care pharmacy practice, home health care practice and hospice practice. Members are also involved in academia and some work for pharmaceutical manufacturers. While it is not possible to quantify the actual number of APhA's members who engage in drug compounding activities on a regular basis, virtually all practicing pharmacists will be involved with compounding activities at some point during their career.

APhA has a compelling interest in ensuring a pharmacist's right to compound drug formulations to meet the needs of patients, in collaboration with practicing physicians,[2] as part of the health care giving team. Pharmacists' compounding activities are a critical component of the American health care system, allowing physicians to prescribe medication therapy to best meet the needs of their patients. APhA submits this brief to protect the interests of its members, the interests of all pharmacists who now, or in the

---

[1] Petitioners and Respondents have consented to the filing of this brief *amicus curiae*. The consents have been filed with the Clerk of this Court. No part of this brief has been authored by counsel for either party. No persons other than the *amicus curiae*, its members or their counsel made a monetary contribution to the preparation and submission of this brief.

[2] Physicians do not have an exclusive domain in prescribing medications: dentists, advanced practice nurses, physician assistants and other health professionals may also prescribe medications in some states. The term "physician" is used in this brief to refer to physicians and other health care professionals with privileges and responsibilities related to prescribing drug therapy.

future may, engage in the practice of compounding drugs to meet the needs of their patients and the requirements of the physician, all in furtherance of the physician/pharmacist/patient relationship. We hope in this brief to highlight the importance and major contribution that compounding by the pharmacy profession brings to the drug delivery and medication use process in the United States.

SUMMARY OF ARGUMENT

Compounding of medications for patient use has been a significant component of the practice of pharmacy and medicine since time immemorial. It has traditionally been characterized by the physician/pharmacist/patient relationship wherein professionals work together to individualize care for the maximum benefit of the patient. Compounding is performed by a licensed pharmacist, physician or other qualified health care professional. It has routinely involved the formulation of individualized treatment in response to a valid prescription from a physician or in response to a reasonably anticipated prescription based upon prior experience and expected needs of individual patients. Pharmacy compounding is performed on the site of the pharmacy for nearly immediate dispensing and use by, or administration to, the patient. The profession's definition of compounding does not encompass the preparation of massive amounts of a drug product with the contemplation of distribution to a mass market of unknown users in unknown venues.

These characteristics of pharmacy compounding were extant when Congress passed the Food, Drug and Cosmetic Act in 1938 ("FDCA"), 21 U.S.C. § 301 *et seq.*, and there was no contemplation in the legislative history that compounding would be limited or prohibited as a result of that statute. In fact, compounding continued without benefit of "authorizing legislation" until 1997 when the traditional characteristics of compounding were codified in the Food and Drug Administration Modernization Act of 1997 ("FDAMA"). 21

U.S.C. § 353a. The significant differences were that FDAMA contained the limitation that prohibited advertising of specific compounded products, and volume limits on products distributed out of state. It is the advertising limitation that is in issue in this case.

The FDCA and the processes it mandates were designed to address the situation where a "new drug" would be developed over time, proved as to its safety and then mass marketed to millions of people throughout the United States.[3] There is an obvious conflict between this concept of a "new drug" and a compounded drug. A compounded drug is one that is formulated for a specific patient need, such as an allergy to an ingredient, that cannot be met by a mass manufactured drug. A compounded drug is used fairly promptly after it is formulated. Because of the limited and specific nature of the compounded formulation, it simply would not be possible for a compounded drug to go through the "new drug" approval process that takes years to accomplish with the expenditure of a large amount of money. To have applied the "new drug" requirements of FDCA to the process of compounding from 1938 going forward would have been tantamount to outlawing compounding, and this, clearly, was neither intended nor occurred.

It is unfounded to suggest that traditional compounding, as detailed above, offers a realistic opportunity to do an "end run" around the "new drug" regulatory system. Even including all compounded drugs in all settings nationwide (hospitals, long-term care facilities, community pharmacies, etc.), compounded drugs account for a very small percent of the total dispensed drugs in the United States. It makes no

---

[3] Subsequent amendments to the act expanded the requirements of a "new drug" to include efficacy. 21 U.S.C. §§ 201(p)(1) and (2); 21 U.S.C. § 355(b), (d) and (e). There existed legislation exempting pharmacists from registration and inspection which further indicates that compounding was not contemplated within the definition of "new drug." *See* 21 U.S.C. § 360(g)(1) and 21 U.S.C. § 374(a)(2)(A).

logical sense to claim, as the government does, that the only distinction between compounding and manufacturing is the limit on the pharmacist's right to advertise a particular prescription drug that he or she is able to compound. This single criterion does nothing to further any governmental interest, especially not its stated concern that without this limitation, pharmacists will be able to do an "end run" around the regulatory process.

Compounding was not illegal before the passage of FDAMA,[4] and is regulated by states as part of their oversight of the practice of pharmacy. While FDAMA attempted merely to codify what pharmacists were already doing in the compounding arena, it introduced for the first time the legally imposed limitation that advertising was not allowed. Pharmacists should not be required to forego their constitutional rights in order to continue to engage in the activities they have been legally engaging in for centuries.

STATEMENT OF FACTUAL CONSIDERATIONS

I. The Practice of Pharmacy

In most communities, pharmacists are the primary providers of pharmaceuticals and pharmaceutical care services to the American public. The critical function that pharmacists provide to patient health care is serving as the medication use specialist whose services increase the effectiveness of drug therapy. Pharmacists fulfill a societal need by increasing the effectiveness of drug therapy and thereby improving patient health outcomes. Moreover, pharmacists are the most accessible health-care professionals and enjoy a high degree of earned trust by the public.

Practicing pharmacists, through their education and licensure, assume an ethical obligation to the public to

[4] The fact that the government makes the argument that compounding was not illegal during the period from 1938 to 1997 because of FDA's *noblesse oblige* is unfounded.

maximize the intended benefits of drug therapy while minimizing the risk of unintended side effects and adverse reactions. In preparing a medication for dispensing, the pharmacist assesses the patient's condition, the appropriate dosage scheduling, and any contraindications of the medication with the patient's other prescriptions or diseases. The pharmacist may provide the patient with information on the potential risks and benefits of the medication and assess the patient's understanding of the prescription instructions in order to achieve an optimal therapeutic outcome.

Pharmacists have the responsibility to deliver to patients individualized packages of medication containing patient-specific instructions, an appropriate quantity of the medication, and essential product information that will allow the patient to use the medication most effectively. Pharmacists have expanded from primarily a product-oriented function, focusing on the accurate production and dispensing of the drug product, to a patient-oriented focus, emphasizing proper use of drug therapy by the patient. Today, pharmaceutical care necessitates a proactive healthcare provider who assumes interactive and participatory responsibilities with the intention of improving outcomes. When manufactured products are not appropriate for a patient, the pharmacist's efforts to provide pharmaceutical care are thwarted unless compounding is an option. Without pharmacy compounding, there would be no medication to dispense, nor any medication therapy to optimize. Compounding enables pharmacists to contribute their medication knowledge and expertise to produce individualized medications that meet these needs and improve health outcomes.

II. Pharmacy Compounding

As a component of monitoring the distribution and use of prescribed drug products, pharmacists compound prescriptions to meet the specific needs of individual patients. Compounding has always been a basic part of pharmacy practices; the drugs, dosage forms, and equipment or techniques have changed as pharmacy practice has advanced.

As A.C. Wooten in *Chronicles of Pharmacy* said, "[p]harmacy, or the art of selecting, extracting, preparing and compounding medicines from vegetable, animal, and mineral substances, is an acquirement that must have been almost as ancient as man himself on earth."[5] The early practice of pharmacy required the compounding of virtually all medications, because there were few, if any, commercially available products. As pharmaceutical companies were founded there became less need for compounding most widely used products, although the need to compound has certainly not disappeared.

Compounding may involve different activities in different pharmacy practice settings. It may mean the preparation of oral liquids, topicals, suppositories; the conversion of one dose or dosage form into another; the preparation of select dosage forms from bulk chemicals; the preparation of intravenous admixtures, parenteral nutrition solutions, pediatric dosage forms from adult dosage forms; the preparation of radioactive isotopes; or the preparation of cassettes, syringes, and other devices with drugs for administration in the home setting. Examples of some of the most common compounded products include lotions, ointments, creams, gels, suppositories, intravenously administered fluids and medications, total parenteral nutrition products, oral suspensions, and troches.

Physicians and pharmacists recognize that some individuals and their healthcare needs do not always fall in the windows of commercially available dosage strength and formulations and that large-scale manufacturers cannot tailor-make a medication for a single patient or a handful of patients in a cost effective manner. Many patients need custom-made medication dosages to solve specific medical problems. Pediatric or geriatric patients may need extremely small

---

[5] Wooten, A.C., *Chronicles of Pharmacy, quoted in* Dinah G. Jordan, *Pharmacist Compounding v. Veterinarian Compounding: Similarities and Differences,* 205 JAVMA 256 (1994).

doses, cancer patients may need specific combinations of chemotherapy drugs to treat their disease, or special dosage forms may be necessary to care for patients with AIDS, chronic pain or other maladies.[6] Some therapies, such as parenteral nutrition, can only be provided to patients using compounded dosage forms. Still other patients need preservative-free products, liquids with special flavors, or delivery systems that are not commercially available.

Some therapies, such as hyaluronidase injection (used to increase dispersion and absorption of other drugs injected under the skin), must be compounded because they generate insufficient revenue to pharmaceutical companies to justify large-scale manufacturing. Additionally, some medications may not have sufficient shelf life to withstand the commercial distribution process and therefore need to be prepared at the time of dispensing, such as radioactive drugs used to diagnose or treat disease. Many manufactured "finished pharmaceutical" products are only "finished" in the sense of being ready to ship and then store in the pharmacy. The products must still be compounded to provide a dosage form suitable for a patient's treatment.

It is a fundamental right of the pharmacy profession to extemporaneously compound quality prescription products for patients who have unique medication needs. The pharmacist may, through understanding of the principles of compounding, recommend drug therapy that is not provided by the pharmaceutical industry but that is individualized for a specific patient's needs at a specific time. For these unique needs, many pharmacists offer compounding services guided by the Good Compounding Practices established by the U.S.

---

[6] The pharmaceutical manufacturers recognize the need for compounding, because they include instructions for compounding specialized dosage forms, such as oral suspensions, in some of their package inserts, which are the instructions for use that accompany any drug product and must be approved prior to distribution by the FDA.

Pharmacopoeia.[7] In providing compounding services, pharmacists work hand-in-hand with physicians to solve problems not addressed by commercially available drugs, and develop a special and unique relationship with the patients they serve.

III. Types of Compounding

Pharmacists possess the unique knowledge and skill required for compounding and preparing medications to meet the unique and immediate needs of a patient. Extemporaneous compounding allows pharmacists the opportunity to use their scientific education and training to individualize patient care through the preparation of patient-specific products.

There are many different circumstances calling for compounded prescriptions, including the isolated, the routine and the batch prepared. The isolated prescription is one that the pharmacist is not expecting to receive nor expecting to dispense again.[8] The routine prescription is one the pharmacist may expect to receive in the future on a routine basis, and there may be some benefits to product quality to standardize these preparations, i.e., preparation protocols on file.[9] The batch-prepared prescription is one in which multiple identical units are prepared as a single operation in anticipation of the receipt of prescriptions.[10] All of these compounding activities have been part of the pharmacy profession for many years.

---

[7] *Pharmacy Compounding Practice & Sterile Drug Products for Home Use*, Rockville, Maryland: U.S. Pharmacopeia, 1996. The U.S. Pharmacopoeia is an official compendium of drug information recognized by the FDCA.

[8] 21 U.S.C. § 503a (a)(1)(A) and (B).

[9] 21 U.S.C. § 503a (a)(2)(A).

[10] 21 U.S.C. § 503a (a)(2)(B).

A. Compounding in Cancer Treatment

One of the most important clinical needs for compounding occurs in the care of patients with cancer. Almost all chemotherapy involves drugs and drug combinations that are compounded by pharmacists. It is imperative that a patient receive the correct drug dosage based upon the patient's body size, the type of cancer, the size and type of tumor, and the clinical condition of the patient. This can only be accomplished using compounded patient-specific medication preparations.

B. Compounding for Pediatric Patients

The compounding of pediatric dosage forms has also been an area of extensive activity, particularly in pediatric hospitals, because many drugs used in pediatric treatment are not available in dosage forms appropriate for pediatric patients. Consequently, commercial products manufactured for use in adults must be modified and compounded for use in children. It has been estimated that more than 40% of doses given in pediatric hospitals require compounding to prepare a suitable dosage form. Indeed, utilization of compounded medications is essential for the provision of medical care to hospitalized children.

C. Compounding in Hospitals

In the hospital setting, one of the biggest challenges is to provide individualized dosages specifically directed to the unique needs of each patient. Extemporaneous compounding services within the hospital pharmacy allow the hospital's physicians, nurses and pharmacists to meet this challenge. In particular, intravenous admixtures are compounded because they need to be highly individualized and facilitate administration of drugs not suitable for other routes of administration. It is not practical for a manufacturer to make numerous slightly different products to address the entire range of patients' needs. Generally, only a few or even one dosage form will be commercially viable. However, the commercial form could be used in compounding the myriad

of concentrations and combinations used to meet patients' needs in the hospital setting.

Hospital pharmacists have always utilized their compounding skills to serve the needs of their patients. Because daily intravenous therapy is provided through compounding of medications, nearly every person who has ever been admitted to a hospital has received a compounded product, including those patients receiving outpatient surgery. In fact, the immediate availability of extemporaneous compounding provides the hospital physician with literally any form or strength of medication needed for a specific situation.

D. Compounding in Hospice Care

Hospice programs provide care for patients near the end of their lives. The goal is to enable each patient to make the choices that will provide the best quality of life during the last weeks or months of life. It is a special type of care designed to assist patients to carry on their lives comfortably by managing symptoms, controlling pain, and allowing them to spend their last days with dignity either at home or in a home-like setting. The compounding component of pharmaceutical care is a natural component of hospice care resulting in an enhanced quality of patient care.

Hospice services are for patients who can no longer benefit from curative treatment and generally have a life expectancy of six (6) months or less. About 60% to 70% of hospice patients have cancer and experience debilitating, intractable pain, severe anxiety and depression and have social, psychological, and financial concerns. Hospice pharmacists devise drug therapy protocols that establish optimal pain and symptom control often using compounded dosage forms and enhance patient compliance through patient

education, and monitor patient outcomes in a supportive and humanistic fashion."

Medications to alleviate pain and to control nausea and vomiting are the most common prescriptions for patients in the hospice setting. If commercial products that provide the precise dose(s) required are not available, they can often be supplied by extemporaneous compounding. Patient-specific formulations and dosage forms are constantly being developed by compounding pharmacists to meet the needs of these patients. One of the problems for many hospice patients is that pain medications are not manufactured in the required dosages. Additionally, patients often are not physically capable of swallowing the number of commercially manufactured tablets required. A pharmacist can compound a stronger product by transforming a tableted dosage form into a liquid that is easily swallowed. Often patients cannot take any medication by mouth, and often their veins are not accessible to inject medications. In these situations, physicians and pharmacists must modify traditional medications into products that may be applied topically or delivered rectally. Pharmacists engaged in compounding are important in hospice care and their role will undoubtedly continue to evolve and expand in the future.

IV. Preparation of Compounded Pharmaceuticals-Regulatory Changes

The practice of pharmacy has been historically regulated at the state level. Traditional compounding has been considered an integral part of the practice of pharmacy, and therefore, has been appropriately regulated by state boards of pharmacy. A review of state laws reveals that all 50 states

---

[11] *Hospice Care and the Pharmacist,* 1 International Journal of Pharmaceutical Compounding 11 (January/February 1997).

and the District of Columbia describe compounding in their pharmacy practice laws. [12]

NABP's Model State Pharmacy Act defines "practice of pharmacy" to include compounding of drugs and devices. Specifically, "practice of pharmacy" is the:

> "[I]nterpretation, evaluation, and implementation of Medical Orders: the Dispensing of Prescription Drug Orders; participation in Drug and Device selection, Drug Administration, Drug Regimen Reviews...and the responsibility for Compounding and Labeling of Drugs and Devices..."[13]

The Model Act defines "compounding" in terms of preparation of drugs and devices:

> "Compounding" means the preparation, mixing, assembling, packaging, or Labeling of a Drug or Device (i) as the result of a Practitioner's Prescription Drug Order or initiative based on the practitioner/patient/pharmacist relationship in the course of professional practice, or (ii) for the purpose of, or as incident to, research, teaching, or chemical analysis and not for sale or Dispensing. Compounding also includes the preparation of Drugs or Devices in anticipation of Prescription Drug Orders based on routine, regularly observed prescribing patterns."[14]

---

[12] See *NABPLAW® Pharmacy law database, NABP's database of state pharmacy practice acts and regulations.*

[13] Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy, § 104 (1998).

[14] *Id.*, § 105(f).

The Model Act associates compounding with a "prescription drug order," which is defined as "a lawful order from a Practitioner for a Drug or Device for a specific patient."[15]

Most state boards of pharmacy are in the process of or have completed full revisions of their pharmacy practice acts to expand the role of pharmacists.[16] These changes have given pharmacists the opportunity to engage in innovative practices and to promote patient health. Through their pharmacy practice laws, states recognize and regulate compounding as part of the practice of pharmacy.

In short, statutes and regulations are enacted in every state to deal effectively with compounding as part of pharmacy practice. Restricting free speech will not add to the effectiveness of these statutes and regulations any more than it would add to the government's enforcement arsenal in this case. The proposed solution and the problem are simply unrelated.

ARGUMENT

I. Compounding Is Not Manufacturing

At the very heart of the dispute giving rise to this case is the apparent confusion in trying to determine the difference between compounding and manufacturing. Compounding has been defined by the National Association of Boards of Pharmacy ("NABP"):

> **Compounding** - The preparation, mixing, assembling, packaging, or labeling of a drug or device (i) as the result of a practitioner's

---

[15] The NAPB *Good Compounding Practices Applicable to State Licensed Pharmacies* includes a provision restricting a pharmacist's solicitation of specific drug products. However, such a state level provision does not make the advertising prohibition Constitutionally defensible.

[16] Knowlton, C.H., *J APhA* 1997; NS 37 (3):361.

> Prescription Drug Order or initiative based on the pharmacist/patient/prescriber relationship in the course of professional practice or (ii) for the purpose of, as an incident to research, teaching, or chemical analysis and not for sale or dispensing. Compounding also includes the preparation of drugs and devices in anticipation of Prescription Drug Orders based on routine, regularly observed patterns.[17]

Stated simply, the purpose of compounding by a pharmacist is to prepare an individualized drug treatment for a patient based on an order from a duly licensed prescriber. Manufacturing of a drug is defined as follows:

> **Manufacturing** - The production, preparation, propagation, conversion or processing of a Drug or Device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis, and includes any packaging or repackaging of the substance(s) or Labeling or relabeling of its container, and the promotion and marketing of such Drugs or Devices. Manufacturing also includes the preparation and promotion of commercially available products from bulk compound for resale by pharmacies, Practitioners, or other Persons.[18]

The fundamental difference between compounding and manufacturing is the existence of a pharmacist/ prescriber/patient relationship that controls the preparation of the drug product. Compounded drugs are not for resale, but rather, are personal and responsive to the patient's immediate needs. They are produced and administered by the patient's health care professionals, which allows for the monitoring of

---

[17] *Good Compounding Practices Applicable to State Licensed Pharmacies*, Subpart A. Park Ridge, IL:NABP, 1993.

[18] *Id.*

patient outcomes. The compounded drug may be assigned a very short expiration date and the pharmacist may personally advise his patients to immediately report any physical change in the compounded prescription as well as any adverse reactions.

On the other hand, drug manufacturers produce batches consisting of millions of dosage units, such as tablets or capsules, for resale utilizing many personnel and large scale manufacturing equipment. These products are distributed through the normal channels of interstate commerce to individuals unknown to the company. Manufactures are not required to, and do not, provide oversight of individual patients. Federal regulation of large-scale commercial manufacturing is intended to prevent the production of large quantities of ineffective or dangerous manufactured drugs and have them introduced into commerce. Because of the absence of a close relationship with a physician and patient, the manufacturer may remain unaware of a drug's negative effect upon the patients to whom it is administered until larger numbers of adverse effects appear. It is these differences, not advertising, that distinguish compounding from manufacturing.[19]

---

[19] We recognize that the definition of manufacturing includes "promotion" of drug products, whereas the definition of compounding does not. We submit that this does not, however, lead to a valid conclusion that promotion of either compounding or a compounded drug product turns the activity of compounding into manufacturing. Of those states that have adopted some form of the Model Act, only ten (10) include "promotion and marketing" as part of their definition of manufacturing. Alaska Stat. § 8.80.480; Ga. Code Ann. § 26-4-5(23); La. Rev. Stat. Ann. § 1164; Miss. Code Ann. § 73-21-73(q); N.H. Rev. Stat. Ann. § 318.1 (VIII); N.M. Stat. Ann. § 61-11-2.Q.; Okla. Stat. tit. 59, § 353-1(20); S.C. Code Ann. § 40-43-30(29); Tenn. Code Ann. § 63-10-404(18); W. Va. Code Ann. § 30-5-1b(o).

The fundamental differences between manufacturing and compounding are further demonstrated by additional NABP Model Rules, parts of which were eventually codified into the FDAMA of 1997. The NABP Model Rules provide the following:

> "Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions that have been generated solely within an established pharmacist/patient/prescriber relationship, and provided that they maintain the prescriptions on file for all such products compounded at the pharmacy (as required by State law). The compounding of inordinate amounts of drugs in anticipation of receiving prescriptions without any historical basis is considered *manufacturing*...
>
> ...The distribution of inordinate amounts of compounded products pursuant to a legitimate prescription out of state without a prescriber/patient/pharmacist relationship is considered *manufacturing*. Pharmacists engaged in the compounding of drugs shall operate in conformance with applicable State law regulating the practice of pharmacy."[20]

The relationship between the compounding pharmacist and the practitioner provides an appropriate system of checks and balances to make sure that the patient's health is protected and served. A legally compounded prescription by a pharmacist always is authorized by a prescriber. The pharmacist acts as a valuable resource for determining drug compatibility, dosage formulation, etc., to meet the patient's needs and prescriber-intended outcomes, and when

---

[20] *Good Compounding Practices Applicable to State Licensed Pharmacies*, Subpart A, Park Ridge, IL:NABP, 1993. [Emphasis added] (*See also*, 21 U.S.C. § 503a (a)(2)(A) and (B)).

appropriate, may refuse to dispense a prescription calling for compounding that cannot be safely performed. This relationship is the basic difference between compounding and manufacturing, not advertising.

Prior to promulgation of their Compliance Policy Guidelines in the early 1990s and the subsequent enactment of FDAMA, the FDA rarely asserted that compounding was manufacturing. The relevant provisions of FDAMA were promulgated to clarify the inapplicability of the FDCA to compounding.[21] In its brief, the government cites a number of court decisions that, it alleges, equate the traditional compounding of drugs to the manufacturing of "new drugs." *See* Petitioners' Brief at pp. 5 and 6. As the facts in these cases make clear, however, traditional compounding was never at issue in these cases and nor was it ever equated with manufacturing.

In both *United States v. 9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988), and its companion case, *U.S. v. Algon Chemical, Inc.* 879 F.2d 1154 (3rd Cir. 1989), the courts addressed the issue of misbranding of bulk drugs. The misbranding resulted from the fact that the drug labels did not contain "adequate directions for use." The FDA claimed, and both courts concurred, that this misbranding made distribution of the drugs to veterinarians for compounding and use in their practice illegal, so the drugs could be seized by the FDA. In both cases, the courts enjoined the sale of the "misbranded" bulk animal drugs intended for use in compounded veterinarian drug products. *Id.*

It is important to note that neither court decision directly addressed the issue whether the traditional compounding of drugs by pharmacists and physicians equals manufacturing that is "subject to the FDCA's premarket approval process" as contended by the government. See Petitioners' Brief, p. 5. On the contrary, both courts explicitly confirmed the authority

---

[21] S. Rep. No. 43, 105th Cong., 1st Sess., 67-68 (1997).

of a practitioner to compound legally acquired drugs, free from registration and inspection requirements, in the course of his practice. *Algon Chemical*, 879 F.2d at 1160; *Containers*, 854 F.2d at 177, 178.

In another case relied upon by the government, *United States v. Baxter Healthcare Corp.*, 901 F.2d 1401 (7th Cir. 1990), the FDA successfully challenged a program, operated by a recognized drug manufacturer through its regional drug preparation center, involving the reconstitution, repackaging, freezing, and distribution of already approved drugs to healthcare providers without specific FDA approval for the manufacturing of "new drugs." In analyzing the pertinent facts, the court determined that the respondents, by transforming powders and concentrates on a large scale into dosage packages that were not prepared pursuant to a patient-specific prescription and were suitable for immediate use by healthcare providers without further reconstitution or dilution, were operating a manufacturing operation that required "new drug" approval from the FDA. *Id.* In *Baxter Healthcare*, the court was not faced with the issue of traditional compounding of drugs by pharmacists or physicians, but rather, it was faced with the clear manufacturing of drugs subject to FDA regulation.

In reaching its conclusion, the court noted the distinction drawn by Congress between the commercial manufacturing of drugs and the reconstituting (or compounding) of drugs performed by pharmacists and physicians. *Baxter Healthcare*, 901 F.2d at 1409, 1411. The court noted that Congress, through the FDCA, intended to protect the traditional compounding of drugs from FDA regulation by saying:

> "As a policy choice, Congress has exempted pharmacies and physicians from the registration and inspection requirements that apply to all manufacturers of drugs. 21 U.S.C. §§ 360(g)(1), (2), 374(a)(1), (2). The FDA only follows that lead by focusing on the mass commercial distribution of drugs rather than at the individual level of hospitals

> and pharmacists. This does not suggest that the FDA has taken a path which is 'manifestly contrary to the statute,' *Chevron*, 467 U.S. at 844, 104 S.Ct. at 2782, but to the contrary suggests sound adherence to congressional intent."

Id. at 1411.

In *Professionals and Patients for Customized Care v. Shalala*, 56 F.3d 592 (C.A. 5 (Tex.), 1995), the court was called upon to address the issue as to whether the FDA's Compliance Policy Guide constituted a substantive rule of law issued by the agency without benefit of the Administrative Procedure Act, or whether it was, as billed, a policy guide. Both the lower court, *Professionals and Patients for Customized Care v. Shalala*, 847 F.Supp. 1359 (S.D. Texas, 1994), and the appellate court, *Professionals*, 56 F.3d 592 (C.A. 5 (Tex.) 1995), concurred that it was nothing more than an internal guide for the FDA's enforcement efforts. The governments citation of this case at the appellate level for the proposition that "compounded drugs are 'new drugs' subject to the FDA's premarket approval requirements" seems to overstate the holding in the case. In fact, the footnote referred to by the government merely points out that the FDCA does not exempt pharmacies or compounded drugs from its provisions. The court did note that the FDA has not historically brought enforcement actions against pharmacies engaged in traditional compounding, while at the same time, the court recognized that pharmacies that practice traditional compounding are regulated primarily by the states and are exempt from FDA registration requirements and inspections. *Professionals*, 56 F.3d at 594 (*see also* 21 U.S.C. § 360(g)(1) and 21 U.S.C § 374 (a)(2)(A)).

On the other hand, the facts in *United States v. Sene X Eleemosynary Corp.*, 479 F.Supp. 970 (S.D. Fla. 1979), clearly demonstrate a situation where a "manufacturer" is trying to look like a traditional pharmacy and failed to do so. In that case, a corporation compounded a line of products as its only "pharmacy" activity, and distributed those products

interstate in large quantities without the existence of any real pharmacist/patient/physician relationship. Prescriptions were written and delivered by mail from physicians unknown to the patient. Without resolving whether customary or usual acts of pharmacy were exempt from the FDCA's "new drug" provisions, the court swiftly determined that the corporation's actions did not constitute the practice of pharmacy by saying:

> "The question of whether the customary or usual practice of pharmacy is exempt from the Act's new drug provisions need not be resolved in this case, for the means by which the defendants compound, promote, and ultimately distribute GH-3 constitute something wholly apart from the normal practice of pharmacy."

Id. at 978.

As the case law cited by the government makes clear, no court has held that the traditional compounding of drug products by a pharmacist or physician constitutes the manufacturing of drugs subject to FDCA regulation. The government has not and cannot put forth case law that involves the type of traditional compounding at issue in this case.

II. A Compounded Drug Product is not a "New Drug" as Contemplated in FDCA & FDAMA

Compounding of drug products by pharmacists and physicians does not constitute the manufacturing of "new drugs." Historically, while the FDA has subjected "new drugs" to its stringent statutory requirements, pharmacists have continued the traditional compounding of drugs without interference from the FDA. In its Petition, however, the government takes a quantum leap by equating the advertisement of a prescription drug product with manufacturing. *See* Petitioners' Brief at pp. 14, 15. It claims that a pharmacist's advertisement of a specific compounded drug automatically transforms that pharmacist into a manufacturer of "new drugs." While the government clearly

grasps the value and essentials of compounding, it now claims that the advertising of particular compounded drugs creates a loophole in the "new drug" approval process, and therefore, that such activity must be subject to all of FDA's new drug regulations. *See* Petitioners' Brief at pp. 24-26, 32-37, 40, and 41. The government's argument is completely lacking in merit.

A. The Federal Food, Drug & Cosmetic Act of 1938

Congress adopted the Federal Food, Drug & Cosmetic Act in 1938 ("FDCA") to regulate the sale of manufactured drugs to the general public. 21 U.S.C. § 301 *et seq.* As part of this legislation, no 'new drugs' could be introduced into interstate commerce unless they first underwent testing and were approved as safe by the FDA. Section 505(a) of the 1938 regulation (later codified as 21 U.S.C. § 355(a)) provided that: "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an application filed pursuant to subsection (b) is effective with respect to such drug." There is no indication that Congress, the states, pharmacists, or the FDA in 1938 or in the decades that followed believed that compounding of a drug by a pharmacist constituted the introduction of a 'new drug' into the marketplace, regardless of whether the drug was given to the patient in the pharmacy or mailed via interstate commerce to an individual patient. We contend that this is for obvious reasons.

At the time the Act was adopted, there were not very many manufactured drugs available, though the prevalence of manufactured drugs was on the increase. It was, in fact, this increased prevalence of manufactured drugs, as compared with compounded drugs, that formed, at least in part, the impetus for enactment of the FDCA. Following adoption of the FDCA, pharmacists continued to compound without submitting new drug applications. The FDA did not attempt to impose the new drug application requirements upon such pharmacy compounding. Indeed, as a practical matter, given the stringency of new drug application requirements, the

relatively large patient population, and the substantial time and monetary investment required, it would have been all but impossible for pharmacists to meet those requirements had they attempted to do so.

Accordingly, the lack of evidence to the contrary suggests that no one in 1938 viewed section 505 of the FDCA as placing any limitation on compounding. If compounded drugs were to be subjected to the "new drug" requirements of the FDCA, this would have been tantamount to the outlawing of compounding, and the supply of compounded medications to the American public would have been brought to a virtual halt. It is inconceivable that Congress intended to deem all compounding to be illegal, and it is even more unlikely that Congress would have taken this drastic step without explicitly saying so.

B. The Food and Drug Administration Modernization Act of 1997

In 1997, FDAMA was enacted, essentially codifying the general practices involved in compounding that had taken place for many years. FDAMA recognizes the value of compounding and continues to permit pharmacists to compound drugs under the same conditions as traditionally recognized by state regulators and the FDA. FDAMA requires, in relevant part, that: 1) compounding be performed by a licensed pharmacist or physician for the benefit of an identified patient and a) be based upon a valid, unsolicited prescription from a practitioner licensed to prescribe drugs; or b) compounded in limited quantities before receipt of a valid prescription order based upon a history of receiving valid prescription orders from an established pharmacist/physician/patient relationship. 21 U.S.C. § 353a (a); and 2) the pharmacist does not compound regularly or in inordinate amounts drug products that are essentially copies of a commercially available drug product. 21 U.S.C. § 353a(b)(1)(D).

The new conditions, in relevant part, that FDAMA places upon the compounding of drugs that were not a part of "traditional compounding" include: 1) the pharmacist may "not advertise or promote the compounding of any particular drug, class of drug, or type of drug," *see* 21 U.S.C. § 353a(c); 2) the compounded drug product may not be a drug product that presents difficulties for compounding that would adversely affect safety or efficacy, *see* 21 U.S.C. § 353a(b)(3)(A); and 3) the pharmacist or physician may distribute interstate only limited quantities of compounded drugs, *see* 21 U.S.C. § 353a(b)(3)(B).

Contrary to the government's assertion, the new advertising limitation in FDAMA should not transform the compounding of a prescription drug product into the manufacturing of a "new drug." Certainly, there is a substantial government interest in precluding persons or organizations from avoiding the stringent approval process for new drugs by claiming they are merely compounding. As described above, it defies logic to contend that this interest is in any way advanced by limiting the right of a pharmacist in the lawful exercise of his profession to advertise the availability of a particular compounded drug product.

Surrendering a constitutional right should not be the price one has to pay in order to meet the government's substantial interest of avoiding "end runs" around the "new drug" regulatory process. FDAMA includes numerous conditions on the practice of compounding that directly and realistically address the true features of compounding and are more than sufficient to meet the government's objectives in preventing the subversion of the "new drug" approval requirements. FDAMA specifically requires that a compounded drug product be comprised from a list of approved drug substances, *see* 21 U.S.C. § 353a(b)(1); and restricts the compounding of a drug product that has been removed from the market because it has been determined to be unsafe or not effective, *see* 21 U.S.C. § 353a(b)(1)(C). The Act further restricts a compound drug product identified

by regulation as presenting difficulties for compounding that would adversely affect safety or efficacy, *see* 21 U.S.C. § 353a(b)(3)(A).

The government contends in its brief that advertising is the primary indicia of manufacturing as compared to compounding. *See* Petitioners' Brief at pp. 14-16; 33-35. We contend on the contrary that advertising is not the linchpin that, standing alone, can turn compounding into manufacturing. In fact, advertising of a specific compounded product is totally neutral to the issue of compounding versus manufacturing.

CONCLUSION

For the reasons stated above, the Court should declare the solicitation and advertising prohibitions contained in 21 U.S.C. § 353a(a) and (c) (Supp. V 1999) unconstitutional.

Respectfully submitted,

SUSAN C. WINCKLER
AMERICAN PHARMACEUTICAL ASSOCIATION
2215 CONSTITUTION AVENUE, NW
WASHINGTON, DC 20037

MICHAEL H. MCCONIHE
COUNSEL OF RECORD

KEVIN A. KERNAN
O'BRIEN, BUTLER, MCCONIHE & SCHAEFER, PLLC
888 17TH STREET, NW
SUITE 1000
WASHINGTON, DC 20006
(202) 298-6161

COUNSEL FOR AMICUS CURIAE AMERICAN PHARMACEUTICAL ASSOCIATION

Supreme Court, U.S.
FILED
JAN 17 2002

No. 01-344

In the Supreme Court of the United States

TOMMY G. THOMPSON, SECRETARY OF HEALTH AND HUMAN SERVICES, ET AL.

Petitioners,

v.

WESTERN STATES MEDICAL CENTER, ET AL.

Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Ninth Circuit

BRIEF AMICUS CURIAE OF NATIONAL COMMUNITY PHARMACISTS ASSOCIATION IN SUPPORT OF RESPONDENTS

JOHN M. RECTOR
General Counsel
National Community Pharmacists Association
205 Daingerfield Road
Alexandria, VA 22314
(703) 683-8200

KENNETH S. GELLER*
BRITTON B. GUERRINA
Mayer, Brown & Platt
1909 K Street, N.W.
Washington, D.C. 20006
(202) 263-3000

* *Counsel of Record*

BEST AVAILABLE COPY

43 pp

QUESTION PRESENTED

Whether provisions of the Food and Drug Administration Modernization Act of 1997 that permit pharmacist compounding only if the pharmacist "does not advertise or promote the compounding of any particular drug, class of drug, or type of drug" violate the First Amendment.

TABLE OF CONTENTS

Page

QUESTION PRESENTED I

TABLE OF AUTHORITIES iv

INTEREST OF THE AMICUS CURIAE 1

STATEMENT 2

A. Pharmacist compounding has a long, proud history 2

B. Pharmacist compounding and drug manufacturing have long existed side by side 6

C. Millions of patients need pharmacist-compounded drugs 8

D. Pharmacist compounding is legal 10

SUMMARY OF ARGUMENT 15

ARGUMENT 16

BY RESTRICTING ADVERTISING CONCERNING LAWFUL CONDUCT, SECTION 503A VIOLATES THE FIRST AMENDMENT 16

A. Strict scrutiny is the proper standard of review ... 16

B. Section 503A cannot survive strict scrutiny 22

1. The government's asserted goals can be achieved without infringing on pharmacists' fundamental right to free speech 23

2. The speech restrictions are overbroad 24

3. The government's arguments make no sense even on their own terms 27

4. The government cannot regulate conduct indirectly by restricting truthful commercial speech 27

CONCLUSION 29

TABLE OF AUTHORITIES

Page(s)

Cases:

44 Liquormart, Inc. v. *Rhode Island*, 517 U.S. 484 (1996) ..... *passim*

Bates v. *State Bar of Arizona*, 433 U.S. 350 (1977) .. 25, 28

Carey v. *Brown*, 447 U.S. 455 (1980) 21

Carey v. *Population Servs., Int'l*, 431 U.S. 678 (1977) 20, 21

Cedars N. Towers Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder], Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978) 13, 24

Central Hudson Gas & Electric Corp. v. *Public Service Commission of New York*, 447 U.S. 557 (1980) ..... *passim*

Chisom v. *Roemer*, 501 U.S. 380 (1991) 12

City of Cincinnati v. *Discovery Network, Inc.*, 507 U.S. 410 (1993) 17, 21

FDA v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000) 13

Florida Bar v. *Went for It, Inc.*, 515 U.S. 618 (19[illegible] ... 17

Friedman v. *Rogers*, 440 U.S. 1 (1979) 17

Greater New Orleans Broad. Ass'n, Inc. v. *United States*, 527 U.S. 173 (1999) 19

Harrison v. *PPG Indus., Inc.*, 446 U.S. 578 (1980) 12

TABLE OF AUTHORITIES — Continued

Page(s)

Linmark Assocs., Inc. v. *Willingboro Township*, 431 U.S. 85 (1977) 21

Lorillard Tobacco Co. v. *Reilly*, 121 S. Ct. 2404 (2001) 19

Ohralik v. *Ohio State Bar Ass'n*, 436 U.S. 447 (1978) 17

Posadas de Puerto Rico Assocs. v. *Tourism Co.*, 478 U.S. 328 (1986) 18

R.A.V. v. *City of St. Paul*, 505 U.S. 377 (1992) .. 20, 21, 22

Rosenberger v. *Rector & Visitors of Univ.*, 515 U.S. 819 (1995) 21

Rubin v. *Coors Brewing Co.*, 514 U.S. 476 (1995) 28

Texas v. *Johnson*, 491 U.S. 397 (1989) 21

United States v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979) 12, 24

Virginia State Bd. of Pharmacy v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976) ..... *passim*

Western States Medical Ctr. v. *Shalala*, 69 F. Supp. 2d 1288 (D. Nev. 1999), *aff'd in part, rev'd in part*, 238 F.3d 1090 (9th Cir. 2001). 22

TABLE OF AUTHORITIES — Continued

Page(s)

Statutes, Legislative History and Court Rules:

Federal Statutes

21 U.S.C. § 321 ..... 5, 10

21 U.S.C. § 353a 2, 6, 16

21 U.S.C. § 355 11

State Statutes

Ala. Code § 34-23-1 14

Alaska Stat. § 08.80.480 14

Ariz. Rev. Stat. § 32-1901 14

Ark. Code Ann. § 17-92-101 14

Cal. Bus. & Prof. Code § 4037 14

Colo. Rev. Stat. § 12-22-102 14

Conn. Gen. Stat. § 20-571 14

Del. Code. Ann. tit. 24, § 2502 14

Fla. Stat. ch. 465.003 14

Ga. Code. Ann. § 26-4-4 14

Haw. Rev. Stat. § 461-1 14

Idaho Code § 54-1704 14

225 Ill. Comp. Stat. 85/3 14

Ind. Code § 25-26-13-2 14

Iowa Code § 155A.3 14

Kan. Stat. Ann. § 65-1626a 14

TABLE OF AUTHORITIES — Continued

Page(s)

Ky. Rev. Stat. Ann. § 315.010 14

La. Rev. Stat. Ann. § 1164 14

Mass. Gen. Laws ch. 94, § 187 14

Mass. Gen. Laws ch. 94C, § 1 14

Md. Code Ann. 12-101 14

Me. Rev. Stat. Ann. § 13702 14

Mich. Comp. Laws § 33.17707 14

Minn. Stat. § 151.01 14

Miss. Code Ann. § 73-21-73 14

Mo. Rev. Stat. § 338.010 14

Mont. Code Ann. § 37-7-101 14

Neb. Rev. Stat. § 71-1,142 14

Nev. Rev. Stat. § 639.0124 14

N.H. Rev. Stat. Ann. § 318.1 14

N.J. Stat. Ann. § 13:39-1.2 14

N.M. Stat. Ann. § 61-11-2 14

N.Y. Educ. Law § 6801 14

N.C. Gen. Stat. § 90-85.3 14

N.D. Cent. Code. § 43-15-01 14

Ohio Rev. Code Ann. § 4729.01 14

Okla Stat. tit. 59, § 353.1 14

Or. Rev. Stat. § 689.015 14

TABLE OF AUTHORITIES — Continued

Page(s)

63 Pa. Cons. Stat. Ann. § 390-2 14

R.I. Gen. Laws § 5-19-19 14

S.C. Code Ann. § 40-43-30 14

S.D. Codified Laws § 36-11-2.2 14

Tenn. Code Ann. § 63-10-404 14

Tex. Occ. Code Ann. § 551.003 14

Utah Code Ann. § 58-17a-102 14

Va Code Ann. § 54.1-3300 14

Vt. Stat. Ann. tit. 26, § 2022 14

Wash. Rev. Code § 18.64.011 14

W. Va. Code § 30-5-1b 14

Wisc. Stat. § 450.01 14

Wyo. Stat. Ann. § 33-24-124 14

Legislative history

S. Rep. No. 75-91 (1937) 11

S. Rep. No. 75-152 (1937) 11

S. Rep. No. 105-43 (1997) 14

S. 3073, 75th Cong. (2d Sess. 1938) 11

Rules

S. Ct. Rule 37.6 1

TABLE OF AUTHORITIES — Continued

Page(s)

Miscellaneous:

Accreditation Standards and Guidelines for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree (Adopted June 14, 1997), Standard 10.a 15

American Association of Colleges of Pharmacy Center for the Advancement of Pharmaceutical Education, *Educational Outcomes* (Nov. 15, 1998), § I(E)(2) 15

American Institute of the History of Pharmacy homepage, <http://www.pharmacy.wisc.edu/aihp/> (visited Jan. 9, 2001) 6

Winda Benedetti, *Masters of the mortar and pestle*, Spokesman Rev. (July 4, 1999) 9

Amy Calder, *Oakland pharmacy not generic*, Morning Sentinel (May 16, 1997) 10

David F. Cavers, *The Food, Drug, and Cosmetic Act of 1938: Its Legislative History and Its Substantive Provisions*, 6 J. L. & Contemp. Probs. 2 (1939) 11

Roscoe Collins Clark, *Threescore Years and Ten: A Narrative of the First Seventy Years of Eli Lilly and Company 1876-1946* (1946) 4

The Compact Oxford English Dictionary (2d ed. 1991) 3

David L. Cowen & William H. Helfand, *Pharmacy: An Illustrated History* (1990) ..... *passim*

TABLE OF AUTHORITIES — Continued

Page(s)

Richard A. Deno, Thomas D. Rowe, & Donald C. Brodie, *The Profession of Pharmacy: An Introductory Textbook* (1959) 4

A. Doyle, "Silver Blaze," in *The Complete Sherlock Holmes* (1927) 12

FDA Compliance Guide (CPG) 7132.16 (Mar. 16, 1992) 12

Dixie Farley, *FDA's Global Reach to Protect Public Health*, FDA Consumer 6 (Nov. 1986) 27

Mitchell J. Ghen & John R. Rains, *The Ghen and Rains Physicians' Guide to Pharmaceutical Compounding* (2000) 10

Marmian L. Grimes, *Pharmacist receives national recognition for compounding*, Fairbanks Daily News-Miner (Apr. 3, 1999) 10

Remarks of David A. Kessler, Commissioner of Food and Drugs, Annual Conference of the American Pharmaceutical Association (Mar. 16, 1992) 3

Vincent A. Kleinfeld, *Legislative History of the Federal Food, Drug, and Cosmetic Act*, 50 Food & Drug L. J. 65 (1995) 11

Kremers and Urdang's History of Pharmacy (rev'd by Glenn Sonnedecker, 4th ed. 1976) ... *passim*

Warren E. Leary, *Doctors Given Millions by Drug Companies*, N.Y. Times B13 (Dec. 12, 1990) .. 26

Larry Levitt, *Prescription Drug Trends* (Nov. 2001) 9

TABLE OF AUTHORITIES — Continued

Page(s)

Local Pharmacy Makes Kids' Medicine Taste Sweet, Mt. Prospect J. (Apr. 28, 1999) 10

N.A.R.D. J. 1729 (Sept. 15, 1947) 8

N.A.R.D. J. 946D (June 21, 1948) 8

N.A.R.D. J. 1685 (Oct. 16, 1950) 8

N.A.R.D. J. 1941 (Dec. 1, 1952) 8

NCPA-Pharmacia 2001 Digest (2001) 9

North American Pharmacist Licensure Examination (NAPLEX®) Competency Statements 2.1.0, 2.3.0 15

Chris O'Malley, *Small pharmacies customizing again*, Indianapolis News (Aug. 27, 1996) 9

Ed Reed, *Wet Graves, Hoodoo Men and Sharp Cats: The History of Pharmacy in Louisiana From the Very Beginning* (1989) 4

Joseph P. Shapiro & Stacey Schultz, *Prescriptions: How Your Doctor Makes the Choice*, U.S. News & World Rept. 58 (Feb. 19, 2001) 26

U.S. Drugs Speed to Russian Markets, FDA Consumer 4 (May 1994) 27

United States Pharmacopeia (1820) 7

Melinda Voss, *Made-to-order medications*, Des Moines Register (Oct. 20, 1997) 9

Ashley Wazana, *Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift*, 283 J. Am. Med. Assoc. 373 (2000) 26

TABLE OF AUTHORITIES — Continued

Page(s)

Webster's Third New International Dictionary (1986) 3

BRIEF AMICUS CURIAE OF THE NATIONAL COMMUNITY PHARMACISTS ASSOCIATION IN SUPPORT OF RESPONDENTS

INTEREST OF THE AMICUS CURIAE[1]

The National Community Pharmacists Association (NCPA), which was founded in 1898 as the National Association of Retail Druggists (NARD), represents the owners, managers, and employees of 25,000 independent community pharmacies across the United States. The more than 60,000 independent pharmacists nationwide dispense the majority of the Nation's retail prescription drugs. The NCPA is committed to high-quality patient care and to restoring, maintaining, and promoting the health and well-being of the general public.

The NCPA has vigorously opposed the Food and Drug Administration's assertion of jurisdiction over pharmacy compounding. Ten years ago, on its own behalf and as a member of the Joint Commission of Pharmacy Practitioners, the NCPA (then the NARD) met and exchanged several letters with FDA officials regarding the agency's forays into regulating prescription drug compounding. The NCPA also supported passage of proposed legislation to preserve exclusive state jurisdiction over pharmacy compounding (*e.g.*, the bipartisan Pharmacy Compounding Preservation Act of 1995) and participated actively in the congressional debate leading to the passage of the pharmacy compounding provisions of the Food and Drug Administration Modernization Act of 1997 (FDAMA).

---

[1] Pursuant to Rule 37.6, *amicus* certifies that no counsel for a party authored this brief in whole or in part, and that no person or entity, other than the *amicus*, its members, or counsel, has made a monetary contribution to this brief's preparation or submission.

Letters from the parties consenting to the filing of this *amicus* brief have been lodged with the Court.

The NCPA undertook those legislative efforts and expresses its views to the Court because compounding is an integral part of pharmacist care – particularly as provided by independent community pharmacists. Through compounding, the prescribing physician and pharmacist can decide a proper course of therapy for each individual patient and ensure that the patient's specific needs are met. The NCPA supports the traditional right of the pharmacist to compound and believes that the new Section 503A of the Food, Drug and Cosmetic Act (FDCA), added by FDAMA and codified at 21 U.S.C. § 353a, threatens the very nature of the practice of pharmacy by unlawfully restricting the right of community retail pharmacists to provide truthful, accurate information to physicians and the public regarding the potential benefits of compounded drugs and compounding services.

STATEMENT

In its brief and in the courts below, the government has questioned the legitimacy of pharmacist compounding. The government concedes that traditional compounding is useful to patient care, but maintains that compounding is sometimes simply a guise to skirt the federal food and drug laws. The lengthy history of pharmacist compounding demonstrates that the government's arguments regarding the legitimacy and legality of compounding are overstated. Traditional pharmacist compounding is integral to the practice of pharmacy. Pharmacist compounding serves a unique and invaluable role in patient care that large-scale drug manufacturing cannot fill, as demonstrated by the fact that traditional pharmacist compounding and drug manufacturing have existed side-by-side for several hundred years.

A. Pharmacist compounding has a long, proud history.

Practiced for literally thousands of years, compounding is the very root of pharmacy. Even in ancient times, the ability to manipulate natural materials to create medications was highly

valued.[2] Indeed, the very definition of "pharmacy" demonstrates the central role of compounding to the profession: "Pharmacy: the art or practice of preparing, preserving, compounding, and dispensing drugs * * * ; a place where medicines are compounded or dispensed."[3] It is thus no surprise that compounding is recognized as "the traditional art" of the pharmaceutical profession.[4]

As the profession of pharmacy developed, compounding remained central to the pharmacist's duties. Compounding has been part of American pharmacy since the colonial period.[5] Just

---

[2] David L. Cowen & William H. Helfand, *Pharmacy: An Illustrated History* 20 (1990). In fact, the first recorded medical text, written on clay tablets from Mesopotamia dating from 2100 B.C., provides formulas and directions for compounding. For example, the text instructs the practitioner to "pulverize [the bark of] the apple tree and the 'moon' plant; infuse it with *kushumma* wine; let tree oil and hot [?] cedar oil be spread over it." *Id.* at 19 (emphasis and alterations in original).

[3] *Webster's Third New International Dictionary* 1694 (1986) (emphasis added). See also *The Compact Oxford English Dictionary* 663 (2d ed. 1991) (defining "pharmacy" as "the art or practice of collecting, preparing and dispensing drugs, especially for medicinal purposes; the making or *compounding* of medicines; the occupation of a druggist or pharmaceutical chemist") (emphasis added).

[4] Remarks of David A. Kessler, Commissioner of Food and Drugs, Annual Conference of the American Pharmaceutical Association (Mar. 16, 1992).

[5] For example, the first governor of Connecticut Colony, John Winthrop, Jr., prepared compounds himself and is credited with being one of the first colonists to do pharmaceutical work in North America. *Kremers and Urdang's History of Pharmacy* 153-155 (rev'd by Glenn Sonnedecker, 4th ed. 1976). The first pharmacist to be licensed in North America (in Louisiana in 1770) operated under a regulatory code that required pharmacists to "compound exactly the prescriptions as ordered by the doctor without ever adding anything" and not compound medicines without prescriptions or order drugs on

as in Europe, colonial apothecary shops were lined with shelves full of jars of herbs, minerals, and other drug ingredients, and every pharmacist had on hand the tools to compound the ingredients into medicines, including scales for weighing, crucibles for heating, and mortars and pestles for grinding and mixing.[6] The mortar and pestle are the recognized symbols of the profession of independent pharmacy even today.

The creation and sharing of knowledge regarding the possibilities of pharmaceutical compounding and specific compound drugs have been critical to the development of the profession of pharmacy. Compilations of drug recipes were created even in ancient times. Hippocrates's Corpus Hippocratean mentions drugs, pharmaceutical processes, and dosage forms,[7] and Dioscorides's treatise De materia medica (50-70 A.D.) was used as a reference for centuries.[8] Governments eventually adopted official pharmacopeia, the first of which was published in Nuremberg in 1546.[9] By the nineteenth century, having a well-developed pharmacopeia was a matter of national pride, and countries took care to develop their own lists of official drugs.[10]

---

their own accord. Ed Reed, *Wet Graves, Hoodoo Men and Sharp Cats: The History of Pharmacy in Louisiana From the Very Beginning* 13 (1989).

[6] See, *e.g.*, Kremers & Urdang at 156 (listing materials included in inventory of pharmacist's estate in 1725). See also Roscoe Collins Clark, *Threescore Years and Ten: A Narrative of the First Seventy Years of Eli Lilly and Company 1876-1946* 6-7 (1946) (describing the accoutrements of the pharmacy where Eli Lilly worked as an apprentice).

[7] Richard A. Deno, Thomas D. Rowe, & Donald C. Brodie, *The Profession of Pharmacy: An Introductory Textbook* 43 (1959).

[8] Cowen & Helfand at 29.

[9] *Id.* at 68, 91.

[10] See Cowen & Helfand at 137.

A national pharmacopeia for the United States first emerged with the publication of the United States Pharmacopeia in 1820.[11] Early editions distinguished between manufactured drugs and those to be prepared by individual pharmacists. When the 1882 edition de-emphasized the making and compounding of medications in community pharmacies,[12] pharmacists became concerned that the de-emphasis on compounding would lead to the loss of "one of their principal professional functions."[13] In response, the American Pharmaceutical Association developed the National Formulary. First published in 1888, early editions of the National Formulary emphasized the importance of pharmacist compounding to provide flexibility necessary to meet the needs of individual patients.[14] Both the United States Pharmacopeia and the National Formulary were recognized under federal law in 1906 and again in 1938.[15] They retain official legal status today.[16]

Besides pharmacopeia, which compiled drug descriptions and formulae, other materials aided pharmacists in compound-

---

[11] Kremers & Urdang at 260-263.

[12] *Id.* at 267.

[13] *Id.* at 275-276.

[14] *Id.* at 275.

[15] *Id.* at 276.

[16] *Id.* at 269. See 21 U.S.C. § 321 (defining "drug" to mean "articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them" and "official compendium" to mean "the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, official National Formulary, or any supplement to any of them"). Section 503A also requires pharmacists performing compounding services to comply with the monographs from the United States Pharmacopeia or the National Formulary or the Pharmacopeia's chapter on pharmacy compounding. See 21 U.S.C. § 353a(b)(1)(A)(i)(I).

ing drugs. In 1849, William Procter, Jr., a professor at the Philadelphia College of Pharmacy and the "Father of American Pharmacy,"[17] published Practical Pharmacy: the Arrangements, Apparatus and Manipulations of the Pharmaceutical Shop and Laboratory, based on works of German and British pharmacists.[18] Wilbur L. Scoville published the first edition of The Art of Compounding in 1895. Nine editions of the book were published (the last in 1957).[19] A committee of the American Pharmaceutical Association published The Pharmaceutical Recipe Book, which listed a variety of compounding formulas, in 1929; second and third editions followed in 1936 and 1942.[20] The existence of these materials demonstrates the historic role of compounding in traditional American pharmacy.

B. Pharmacist compounding and drug manufacturing have long existed side by side.

As was the case with many industries and professions, the industrial revolution precipitated many changes in pharmacy, including a gradual de-emphasis on pharmacist compounding. Drug manufacturing began in the United States in the eighteenth century,[21] and took hold in the nineteenth, when pharmacists like Eli Lilly, druggists like Samuel P. Wetherill, and doctors like E.R. Squibb began to mass produce drugs. These and other drug manufacturers, with sophisticated technology and economies of scale, were able to manufacture and distribute many drugs to the local pharmacy. They could also invest

[17] See American Institute of the History of Pharmacy homepage, <http://www.pharmacy.wisc.edu/aihp/> (visited Jan. 9, 2001).

[18] Cowen & Helfand at 143.

[19] Kremers & Urdang at 285.

[20] *Id.* at 281.

[21] Large-scale manufacturing of pharmaceutical chemicals probably first occurred in the United States in 1786 by a firm of wholesale and retail druggists in Philadelphia. See Kremers & Urdang at 326.

money in research to develop new drug combinations and delivery mechanisms (like coated tablets).[22]

Large-scale manufacturing of drugs and drug ingredients was not entirely an advent of the industrial revolution, however. Pharmacopeia often included both instructions for compounding drugs and descriptions of medications manufactured in bulk. For example, one of the earliest American pharmacopeia – the "Lititz pharmacopeia" (1778), a military formulary used in the Revolutionary War – described both medicines to be created in bulk and distributed for use as well as those to be compounded locally in hospital dispensatories.[23] Similarly, the early editions of the United States Pharmacopeia distinguished between manufactured drugs and those to be compounded by local pharmacists.[24]

For many years drug manufacturers and compounding pharmacists worked hand-in-hand. Despite the rapid growth of pharmaceutical manufacturing, until relatively recently most prescriptions continued to be filled through compounding.[25] For example, in the 1920s up to 80 percent of prescriptions required the pharmacist to have a good knowledge of compounding.[26] Thus, even as pharmaceutical manufacturing developed, a

[22] See generally *id.* at 314-315, 328-332; Cowen & Helfand at 175-180.

[23] Kremers & Urdang at 169-170.

[24] Indeed, the preface to the first edition (1820) reflects the emergence of large-scale drug manufacturing: "Those compound substances which are prepared in the large way at manufactories, and which are to be kept by the apothecary, though not necessarily prepared by him, are inserted on the materia medica list. Those which are to be made by the apothecary alone, are placed among the preparations and compositions." Kremers & Urdang at 263 (quoting United States Pharmacopeia at 22 (1820)).

[25] Kremers & Urdang at 315.

[26] Cowen & Helfand at 186.

major component of the drug manufacturing business consisted of providing pharmacies with drug ingredients and formulae for use by pharmacists in compounding.[27]

Over time, however, the proportion of prescriptions requiring compounding or other sorts of professional manipulation by the pharmacist declined and compounding gradually began to play a less central role in American pharmacy. In the early 1930s, 75 percent of prescriptions required a pharmacist trained in compounding. In 1950, 26 percent of prescriptions required compounding, but by 1962 the percentage was less than 5. The number of prescriptions filled through compounding has hovered around 5 percent ever since.[28]

C. Millions of patients need pharmacist-compounded drugs.

Although it is now the exception rather than the norm, pharmacist compounding continues to play a crucial role in public health. Mass-produced, manufactured drugs meet the needs of most patients, but they do not meet the needs of all of them. As pharmacists and physicians have become reacquainted with how compounding can be used to tailor medications to

[27] See, *e.g.*, N.A.R.D. J. 1941 (Dec. 1, 1952) (advertisement by Mallinckrodt Chemical Works for prescription chemicals for use in compounding, including testimonial by experienced compounding pharmacist); N.A.R.D. J. 1685 (Oct. 16, 1950) (advertisement by Mallinckrodt Chemical Works for "compoundable chemicals for precision compounding"); N.A.R.D. J. 946D (June 21, 1948) (advertisement for "Mercurochrome" brand of merbromin, dibromoxymercurifluoresceine-sodium in four forms for pharmacists to use in preparing various solutions); N.A.R.D. J. 1729 (Sept. 15, 1947) (advertisement by Merck & Co. for prescription chemicals).

[28] Kremers & Urdang at 315; *Virginia State Bd. of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 752, 766 (1976) (estimating that in the mid-1970s 5 percent of prescriptions were filled through compounding).

meet the needs of individual patients, compounding has undergone a renaissance. The precise number of prescriptions currently filled through compounding is not known, but estimates vary between 1 and 10 percent of all prescriptions filled. The numbers may appear small as a relative matter, but they indicate that millions of patients require the services of a compounding pharmacist in order to have their medication needs satisfactorily met.[29]

The need for compounding persists for many reasons. Some patients are not able to use a medication in its manufactured form: for example, the dye or lactose coating may trigger an allergic reaction, a pill may be difficult or uncomfortable to swallow, or the dose may be too strong. In these instances, the pharmacist can customize the medication especially for the patient by making it without the dye or lactose,[30] putting it in a different delivery form (such as a transdermal stick or suppository),[31] or lowering the dosage.[32] Sometimes a patient may need a drug that is no longer produced because the manufacturer has gone out of business or the drug is not economical to mass produce; in that case, the independent pharmacist can re-create

[29] In 2000, approximately 3 billion prescriptions were dispensed. See Larry Levitt, *Prescription Drug Trends* chart 3 (Henry J. Kaiser Family Foundation Nov. 2001). Assuming compounding constitutes 1 percent of all prescriptions filled, that means approximately 30 million prescriptions were compounded. Approximately 83 percent of independent pharmacies report that they provide compounding services. See *NCPA-Pharmacia 2001 Digest* 14, 18, 23 (2001).

[30] See, *e.g.*, Chris O'Malley, *Small pharmacies customizing again*, Indianapolis News (Aug. 27, 1996).

[31] See, *e.g.*, Winda Benedetti, *Masters of the mortar and pestle*, Spokesman Rev. (July 4, 1999).

[32] See, *e.g.*, Melinda Voss, *Made-to-order medications*, Des Moines Register (Oct. 20, 1997).

the drug through compounding.[33] Sometimes, as with children, the best way to ensure that the patient complies with the prescription is to mask the medication in a candy-like flavor and form.[34] Compounding can even be useful to medicate finicky pets.[35] Thus, through compounding, pharmacists can ensure that all patients – regardless of their individual needs and circumstances – are able to receive the drug therapies they require.[36]

D. Pharmacist compounding is legal.

The government's argument turns in part on its assertion that all compounded drugs are subject to the new drug approval requirements of the FDCA. In the government's view, the compounding pharmacist "creates a 'new drug' because the compounded product is not 'generally recognized, among experts * * *, as safe and effective.'"[37] The government thus contends that all compounding – even the traditional compounding performed by pharmacists – is subject to the FDCA.[38] However, this understanding of the FDCA's reach is a recent creation.

---

[33] See, *e.g.*, Marmian L. Grimes, *Pharmacist receives national recognition for compounding*, Fairbanks Daily News-Miner (Apr. 3, 1999).

[34] See, *e.g.*, *Local Pharmacy Makes Kids' Medicine Taste Sweet*, Mt. Prospect J. (Apr. 28, 1999).

[35] See, *e.g.*, Amy Calder, *Oakland pharmacy not generic*, Morning Sentinel (May 16, 1997).

[36] See generally Mitchell J. Ghen & John R. Rains, *The Ghen and Rains Physicians' Guide to Pharmaceutical Compounding* 27-29 (2000).

[37] U.S. Br. 4 (quoting 21 U.S.C. § 321(p)(1)).

[38] *Id.* at 4-5, 18-19, 25. Taking the government at its word, if a pharmacist compounds a single dose of a drug in response to a physician's prescription and does not seek FDA approval, that pharmacist is violating the FDCA.

The new drug approval requirements of the FDCA, codified at 21 U.S.C. § 355, were added to the food and drug reform legislation pending in 1937-1938 in response to the deaths of more than 100 people who took a noncompounded drug called "Elixir Sulfanilmide."[39] The history of the new drug provisions indicates that the Sulfanilmide scandal prompted congressional concern regarding the safety of manufactured drugs – particularly those not recognized by the National Formulary or the United States Pharmacopeia. Drugs compounded by pharmacists were not a focus of the congressional or public debate,[40] and nothing in the FDCA legislative history even suggests that pharmacist compounding was covered by the statute.

This is not at all surprising because, at the time the FDCA was enacted, compounding by independent pharmacists was the standard practice by which prescriptions were filled – and continued to be for the next 10 to 20 years.[41] If the FDCA had

---

[39] Although new food and drug legislation had been pending for years when the "Elixir Sulfinalmide" scandal arose, the pending legislation did not provide for safety testing of new drugs. In response to the scandal, language was added to the pending legislation that forbade the introduction into interstate commerce of "any drug * * * not generally recognized as safe for use." David F. Cavers, *The Food, Drug, and Cosmetic Act of 1938: Its Legislative History and Its Substantive Provisions*, 6 J. L. & Contemp. Probs. 2, 20 (1939) (quoting S. 3073, 75th Cong. (2d Sess. 1938)). See also Vincent A. Kleinfeld, *Legislative History of the Federal Food, Drug, and Cosmetic Act*, 50 Food & Drug L. J. 65, 92-93 (1995); Kremers & Urdang at 221.

[40] For example, two Senate reports do not even mention compounding. See S. Rep. No. 75-91 (1937); S. Rep. No. 75-152 (1937). See also Cavers, 6 J. L. & Contemp. Probs. at 32-34, 40 (discussing development and scope of FDCA drug provisions).

[41] In the 1930s when the FDCA was enacted, approximately 75 percent of all prescriptions were filled through pharmacist compounding. See page 8, *supra*. As children of the 1930s

radically overhauled the practice of pharmacy by outlawing compounding, one would expect that those provisions of the FDCA would have received significant attention both in the legislative history and in public discourse. But no evidence of such attention exists. Indeed, for 50 years, no one – not even the FDA – interpreted the FDCA's statutory language to reach traditional pharmacist compounding. Like the dog that did not bark, the silence on this matter indicates that there was, in fact, no such intent.[42]

In short, although since 1992 the FDA has argued that the FDCA provides it with authority to regulate all compounding,[43] the historical understanding of the statute demonstrates that this is not so.[44] Just as the agency attempted unsuccessfully in

undoubtedly remember, filling a prescription sometimes meant observing the local pharmacist make the medication called for in the prescription.

[42] See, *e.g.*, *Chisom* v. *Roemer*, 501 U.S. 380, 396 & n.23 (1991) (likening Congressional silence to "the dog that did not bark") (citing A. Doyle, "Silver Blaze," in *The Complete Sherlock Holmes* 335 (1927)); *Harrison* v. *PPG Indus., Inc.*, 446 U.S. 578, 602 (1980) (Rehnquist, J., dissenting) ("In a case where the construction of legislative language such as this makes so sweeping and so relatively unorthodox a change as that made here, I think judges as well as detectives may take into consideration the fact that a watchdog did not bark in the night.").

[43] See FDA Compliance Guide (CPG) 7132.16 (Mar. 16, 1992).

[44] The government (at 6) points to two counter examples. However, these cases clearly involved large-scale drug manufacturing and thus do not address whether traditional pharmacist compounding falls within the parameters of the FDCA. See *United States* v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970, 978 (S.D. Fla. 1979) ("The question of whether the customary or usual practice of pharmacy is exempt from the [FDCA's] new drug provisions need not be resolved in this case, for the means by which the defendants compound, promote, and ultimately distribute GH-3 constitute something wholly

FDA v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000), the FDA is again using ambiguity in statutory language to expand retroactively a statute into areas where it was never intended to go.[45]

Moreover, the government's reading of the statute borders on the absurd, because it would make little sense to construe the FDCA to require new drug approval every time an individual patient needs a customized drug. Under such a reading, many patients would never receive necessary medication, because it would either never be created (given the cost of the approval process) or be created too late (given the length of the approval process).[46] It is hard to believe that Congress meant the new drug approval process to deprive people with unique needs of necessary (and potentially life saving) pharmacist-compounded drugs.

That traditional pharmacist compounding is legal is further supported by its status in the 50 states. It is the states, of course, not the FDA, that license and regulate pharmacists and individual pharmacies. All of the states treat compounding as

apart from the normal practice of pharmacy."); *Cedars N. Towers Pharmacy, Inc.* v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at ¶ 38,828 (S.D. Fla. Aug. 28, 1978) ("Bulk compounding of drugs at wholesale prices with nationwide distribution is not the type of activity intended to be exempt from registration [as a drug manufacturer].").

[45] See *Brown & Williamson*, 529 U.S. at 146-147 ("[T]here is no evidence in the text of the FDCA or its legislative history that Congress in 1938 even considered the applicability of the Act to tobacco products. Given the economic and political significance of the tobacco industry at the time, it is extremely unlikely that Congress could have intended to place tobacco within the ambit of the FDCA absent any discussion of the matter.") (citation omitted).

[46] See U.S. Br. 26-27.

fundamental to the practice of pharmacy,[47] and compounding is an integral part of every state's definition of pharmacy.[48] In addition, the North American Pharmacist Licensure Examination (NAPLEX®) requires that candidates demonstrate some

[47] Ala. Code § 34-23-1; Alaska Stat. § 08.80.480; Ariz. Rev. Stat. § 32-1901; Ark. Code Ann. § 17-92-101; Cal. Bus. & Prof. Code § 4037; Colo. Rev. Stat. § 12-22-102; Conn. Gen. Stat. § 20-571; Del. Code. Ann. tit. 24, § 2502; Fla. Stat. ch. 465.003; Ga. Code. Ann. § 26-4-4; Haw. Rev. Stat. § 461-1; Idaho Code § 54-1704; 225 Ill. Comp. Stat. 85/3; Ind. Code § 25-26-13-2; Iowa Code § 155A.3; Kan. Stat. Ann. § 65-1626a; Ky. Rev. Stat. Ann. § 315.010; La. Rev. Stat. Ann. § 1164; Me. Rev. Stat. Ann. § 13702; Md. Code Ann. 12-101; Mass. Gen. Laws ch. 94, § 187; ch. 94C, § 1; Mich. Comp. Laws § 33.17707; Minn. Stat. § 151.01; Miss. Code Ann. § 73-21-73; Mo. Rev. Stat. § 338.010; Mont. Code Ann. § 37-7-101; Neb. Rev. Stat. § 71-1,142; Nev. Rev. Stat. § 639.0124; N.H. Rev. Stat. Ann. § 318.1; N.J. Stat. Ann. § 13:39-1.2; N.M. Stat. Ann. § 61-11-2; N.Y. Educ. Law § 6801; N.C. Gen. Stat. § 90-85.3; N.D. Cent. Code. § 43-15-01; Ohio Rev. Code Ann. § 4729.01; Okla Stat. tit. 59, § 353.1; Or. Rev. Stat. § 689.015; 63 Pa. Cons. Stat. Ann. § 390-2; R.I. Gen. Laws § 5-19-19; S.C. Code Ann. § 40-43-30; S.D. Codified Laws § 36-11-2.2; Tenn. Code Ann. § 63-10-404; Tex. Occ. Code Ann. § 551.003; Utah Code Ann. § 58-17a-102; Vt. Stat. Ann. tit. 26, § 2022; Va Code Ann. § 54.1-3300; Wash. Rev. Code § 18.64.011; W. Va. Code § 30-5-1b; Wisc. Stat. § 450.01; Wyo. Stat. Ann. § 33-24-124. See also Sen. Rep. No. 105-43, at 64 (1997).

[48] See, *e.g.*, Ind. Code § 25-26-13-2. ("'Pharmacy' means any facility, department, or other place where prescriptions are filled or compounded[.]"); Iowa Code § 155A.3(24) ("'Pharmacy' means a location where prescription drugs are compounded, dispensed, or sold by a pharmacist[.]"); Ky. Rev. Stat. Ann. § 315.010 ("'Pharmacy' means every place where * * * (b) Prescription drug orders are compounded under the direction of a pharmacist[.]"); Miss. Code Ann. § 73-21-73 ("'Practice of pharmacy' shall mean a health care service that includes, but is not limited to, the compounding, dispensing, and labeling of drugs or devices[.]").

competency in compounding.[49] Compounding also remains part of the standard pharmacy school curriculum.[50] In sum, when independent pharmacists offer and sell compounding services and particular compounded drugs, they are engaging in lawful actions. The FDAMA thus restricts community pharmacists from promoting, advertising, and soliciting completely lawful products and services.[51]

SUMMARY OF ARGUMENT

For many years the FDCA new drug approval requirements (among others) were not applied to traditional pharmacist compounding, and little to no evidence suggests that anyone – pharmacists, physicians, Congress, or the FDA – even contemplated that the FDCA allowed the federal government to prohibit or regulate traditional pharmacist compounding. That

[49] See NAPLEX Competency Statements 2.1.0 ("Perform calculations required to compound, dispense, and administer medication."), 2.3.0 ("Prepare and compound extemporaneous preparations and sterile products.").

[50] The American Council of Pharmaceutical Education (ACPE) accreditation standards include compounding among the professional competencies and outcome expectations for pharmacy students. See *Accreditation Standards and Guidelines for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree* (Adopted June 14, 1997) Standard 10.a ("* * * accurately and safely compound drugs in appropriate dosage forms * * *"). See also American Association of Colleges of Pharmacy Center for the Advancement of Pharmaceutical Education *Educational Outcomes* (Nov. 15, 1998) § I(E)(2) ("Accurately compound individual or bulk medications.").

[51] Even if the "new drug" provisions of the FDCA could be construed to cover the drugs compounded by pharmacists, that alone would not make the practice unlawful. Instead, that would simply mean that the FDA could bring an enforcement action against those pharmacies that shipped inordinate amounts of compounded drugs across state lines.

changed when the FDA began a series of enforcement measures against pharmacies engaged in compounding. In response, Congress attempted to settle any ambiguity regarding the FDCA's scope by expressly exempting pharmacist compounding from various FDCA requirements.[52] However, as a condition of the exemption, Congress required all compounding pharmacists – including those engaged exclusively in traditional compounding – to refrain from advertising or promoting particular compounded drugs or from soliciting business for their compounding services.[53] In so doing, Congress violated the First Amendment.

The district court and the Ninth Circuit struck down Section 503A's speech restrictions as unconstitutional under the balancing test of *Central Hudson Gas & Electric Corp.* v. *Public Service Commission of New York*, 447 U.S. 557 (1980). The district and circuit courts correctly determined that Section 503A is unconstitutional under *Central Hudson*; however, the NCPA urges the Court to review Section 503A under a more exacting standard of review. Strict scrutiny is appropriate in this instance because Section 503A prohibits the dissemination of truthful and accurate information, is not related to the preservation of a fair bargaining process, and restricts speech based on its content and viewpoint. Applying strict scrutiny, Section 503A does not pass constitutional muster.

ARGUMENT

BY RESTRICTING ADVERTISING CONCERNING LAWFUL CONDUCT, SECTION 503A VIOLATES THE FIRST AMENDMENT

A. Strict scrutiny is the proper standard of review.

The government's ability to regulate commercial speech is

[52] See 21 U.S.C. § 353a.

[53] See *id.* § 353a(a), (c).

an extension of its ability to regulate commercial transactions.[54] Regulation of commercial transactions is permitted to ensure that both parties at the bargaining table – and consumers in particular – are treated fairly and that one party does not take advantage of the other. In order to "preserve a fair bargaining process," the government may regulate the information presented to consumers by proscribing false and misleading advertising and mandating the disclosure of additional information in the form of warnings and disclaimers.[55] Similarly, the government may proscribe particular methods or devices for advertising goods and services to prevent consumers from being harassed or unduly influenced, or to prevent their bargaining partners from overreaching.[56] These interests are reflected in the balancing test adopted in *Central Hudson*.[57]

However, since the adoption of the *Central Hudson* balancing test, seven Justices have stated that restrictions of truthful commercial speech should be reviewed under strict rather than intermediate scrutiny. In *Central Hudson* itself, Justice Blackmun noted that the balancing test adopted by the majority "does not provide adequate protection for truthful, nonmisleading, noncoercive commercial speech concerning lawful activities."[58] Justice Brennan expressed similar dissatis

[54] See *Central Hudson*, 447 U.S. at 561; *Friedman* v. *Rogers*, 440 U.S. 1, 10 n.9 (1979); *Ohralik* v. *Ohio State Bar Ass'n*, 436 U.S. 447, 456 (1978).

[55] See *Virginia State Bd. of Pharmacy*, 425 U.S. at 772 n.24.

[56] See *Florida Bar* v. *Went for It, Inc.*, 515 U.S. 618, 630 (1995); *Ohralik*, 436 U.S. at 462.

[57] 447 U.S. at 566.

[58] *Id.* at 573 (Blackmun, J., joined by Brennan, J., concurring in the judgment). See also *City of Cincinnati* v. *Discovery Network, Inc.*, 507 U.S. 410, 431, 436 (1993) (Blackmun, J., concurring) (suggesting that "truthful, noncoercive commercial speech concerning lawful activities is entitled to full First Amendment

faction with the *Central Hudson* test as it applies to prohibitions and regulations of truthful, nonmisleading speech.[59]

In *44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484 (1996), a majority of the Court's current Members concluded that intermediate scrutiny under *Central Hudson* is not appropriate for all commercial speech restrictions. Specifically, Justices Stevens, Kennedy, and Ginsburg rejected the notion that "all commercial speech regulations are subject to a similar form of constitutional review" and concluded instead that "when a State entirely prohibits the dissemination of truthful, nonmisleading commercial messages for reasons unrelated to the preservation of a fair bargaining process, there is far less reason to depart from the rigorous review the First Amendment generally demands."[60] Justice Thomas observed that there is no "historical basis for asserting that 'commercial' speech is of 'lower value' than 'noncommercial speech'" and explained that intermediate scrutiny was inappropriate "at least when, as here, the asserted interest is one to be achieved through keeping would-be recipients of the speech in the dark."[61] Justice Scalia also expressed "discomfort with the *Central Hudson* test" and argued that regulations of commercial speech should be governed according to "the long accepted practices of the American people."[62] *44 Liquormart* thus raised the question of whether intermediate scrutiny applies to *all* regulation of

protection").

[59] See *Posadas de Puerto Rico Assocs.* v. *Tourism Co.*, 478 U.S. 328, 350 (1986) (Brennan, J., joined by Marshall & Blackmun, JJ., dissenting) ("I see no reason why commercial speech should be afforded less protection than other types of speech where, as here, the government seeks to suppress commercial speech in order to deprive consumers of accurate information concerning lawful activity.").

[60] 517 U.S. at 501 (plurality).

[61] *Id.* at 522 (Thomas, J., concurring).

[62] *Id.* at 517 (Scalia, J., concurring in the judgment).

commercial speech or whether intermediate scrutiny applies only when the regulation relates to the governmental interest in preserving a fair bargaining process (by preventing false, misleading, or overbearing speech or speech that relates to unlawful activities).

In two recent cases, the Court expressly noted the uncertain scope of *Central Hudson* and the chorus of calls for its repudiation.[63] However, because in each case the challenged speech restrictions were unconstitutional even under *Central Hudson*'s intermediate scrutiny test, the question whether certain circumstances might justify applying strict scrutiny to (at least) some commercial speech was reserved for another day.[64] This case presents an opportunity to revisit and settle this recurring debate.

Section 503A should be assessed under strict scrutiny for two reasons. First, strict scrutiny applies because Section 503A does not "protect consumers from misleading, deceptive, or aggressive sales practices" or "requir[e] the disclosure of beneficial consumer information," but "prohibits the dissemination of truthful, nonmisleading commercial messages for reasons unrelated to the preservation of a fair bargaining

[63] See *Lorillard Tobacco Co.* v. *Reilly*, 121 S. Ct. 2404, 2421 (2001) ("Petitioners urge us to reject the *Central Hudson* analysis and apply strict scrutiny. * * * Admittedly, several Members of the Court have expressed doubts about the *Central Hudson* analysis and whether it should apply in particular cases."); *Greater New Orleans Broad. Ass'n, Inc.* v. *United States*, 527 U.S. 173, 184 (1999) ("[C]ertain judges, scholars, and *amici curiae* have advocated repudiation of the *Central Hudson* standard and implementation of a more straightforward and stringent test for assessing the validity of governmental restrictions on commercial speech.").

[64] See *Lorillard*, 121 S. Ct. at 2421, 2428; *Greater New Orleans*, 527 U.S. at 184.

process."[65] Because the government has not attempted to justify Section 503A by pointing to any overreaching, undue influence, or fraud that deprives consumers of a "fair bargaining process," under the plurality's test in *44 Liquormart*, strict scrutiny applies.

The Court's decision in *R.A.V.* v. *City of St. Paul*, 505 U.S. 377 (1992), supports the application of strict scrutiny for the same reason. In *R.A.V.*, the Court held that strict scrutiny applies to content-based restrictions that are not related to the "distinctively proscribable content" of the (unprotected) category of speech at issue. Commercial speech is proscribable to the extent it is false, misleading or relates to an illegal activity. Because Section 503A's restrictions are not intended to prevent the dissemination of false or misleading information or otherwise preserve a fair bargaining process (the proscribable content of commercial speech), under *R.A.V.*,"they are presumptively invalid."[66]

Second, strict scrutiny is appropriate because Section 503A's restrictions are content- and viewpoint-based. Under First Amendment principles the Court has long emphasized,

---

[65] *44 Liquormart*, 517 U.S. at 501 (plurality opinion). See also *Carey* v. *Population Servs., Int'l*, 431 U.S. 678, 700 (1977) (noting that a statute that "seeks to suppress completely any information about the price and availability of [a product]" is unconstitutional).

[66] See 505 U.S. at 382-384. As the Court explained, "a State may choose to regulate price advertising in one industry but not in others, because the risk of fraud (one of the characteristics of commercial speech that justifies depriving it of full First Amendment protection) is in its view greater there. But a State may not prohibit only that commercial advertising that depicts men in a demeaning fashion." *Id.* at 388-389 (citations omitted). Similarly, in *44 Liquormart*, four Justices found it "perfectly clear" that a State "could not ban all obscene liquor ads except those that advocated temperance." 517 U.S. at 513 (plurality).

content-based speech restrictions are highly suspect,[67] and viewpoint-based restrictions are even more so.[68] These basic First Amendment principles have been expressed in the commercial speech context,[69] and the Court has invalidated commercial speech restrictions that were impermissibly content based.[70]

There can be no dispute that Section 503A is content-based. It prohibits speech only if it relates to the benefits of particular pharmacist-compounded drugs. Section 503A is also viewpoint-based. It prohibits only that speech that "promotes" com-

---

[67] See, *e.g.*, *R.A.V.*, 505 U.S. at 382 ("Content-based regulations are presumptively invalid."); *Carey* v. *Brown*, 447 U.S. 455, 462-463 (1980) ("Any restriction on expressive activity because of its content would completely undercut the profound national commitment to the principle that debate on public issues should be uninhibited, robust, and wide-open.") (citation and internal quotation marks omitted).

[68] See, *e.g.*, *Rosenberger* v. *Rector & Visitors of Univ.*, 515 U.S. 819, 829 (1995) ("When the government targets not subject matter but particular views taken by speakers on a subject, the violation of the First Amendment is all the more blatant."); *Texas* v. *Johnson*, 491 U.S. 397, 414 (1989) ("If there is a bedrock principle underlying the First Amendment, it is that the government may not prohibit the expression of an idea simply because society finds the idea itself offensive or disagreeable.").

[69] See *44 Liquormart*, 517 U.S. at 499 ("[T]he State retains less regulatory authority when its commercial speech restrictions strike at 'the substance of the information communicated' rather than the 'commercial aspect of [it] – with offerors communicating offers to offerees.'") (quoting *Linmark Assocs., Inc.* v. *Willingboro Township*, 431 U.S. 85, 96 (1977)); *Carey*, 431 U.S. at 701 n.28 (content-based commercial speech regulations "directed not at any commercial aspect of the prohibited advertising, but at the ideas conveyed," violates "the core of First Amendment values").

[70] See, *e.g.*, *Discovery Network*, 507 U.S. at 428-430; *Linmark*, 431 U.S. at 96.

pounded drugs and thus disfavors a particular viewpoint. (The restriction means that large drug manufacturers are free to criticize particular pharmacist-compounded drugs, but pharmacists are prevented from presenting their benefits.) Thus, under settled First Amendment principles, Section 503A should be assessed under strict scrutiny because it suppresses a large amount of truthful commercial speech and threatens to "effectively drive certain ideas or viewpoints from the marketplace."[71]

B. Section 503A cannot survive strict scrutiny.

As explained above, Section 503A prohibits entirely truthful speech informing consumers about the availability of lawful and beneficial pharmacist-compounded drugs. It does not protect consumers from false or misleading commercial speech or speech that is overbearing. The government's interest is not to protect consumers or prevent them from being misled.[72]

Rather, the government claims (at 20-23) that the purpose of Section 503A's speech restriction is to maintain the integrity

[71] *R.A.V.*, 505 U.S. at 387 (citation and internal quotation marks omitted). See also *44 Liquormart*, 517 U.S. at 501 ("Our commercial speech cases have recognized the dangers that attend governmental attempts to single out certain messages for suppression.").

[72] At one point in this litigation, the government argued that Section 503A's speech restrictions are necessary because consumers are ill-equipped to understand and evaluate materials advertising and promoting pharmacist compounding services and pharmacist-compounded drugs and, specifically, might assume that pharmacist-compounded drugs have gone through the FDA approval process. See *Western States Medical Ctr.* v. *Shalala*, 69 F. Supp. 2d 1288, 1299 (D. Nev. 1999), *aff'd in part, rev'd in part*, 238 F.3d 1090 (9th Cir. 2001). The district court rejected this argument because the government presented no evidence to demonstrate that consumers are likely to misunderstand or misinterpret advertising regarding pharmacist-compounded drugs, nor did it show that less restrictive requirements (such as disclaimers) were insufficient to prevent miscommunication. See *id.* at 1299-1300.

of the FDA new drug approval process. According to the government (at 28-29), compounding provides a loophole by which drug manufacturers can directly market their wares to consumers without complying with FDCA requirements (including new drug approval and labeling). The government maintains, in essence, that it must restrict pharmacist speech in order to make that loophole as small and unattractive as possible.[73]

The government contends that restrictions on independent pharmacist speech are critical to its plan because the restrictions will decrease consumer demand for compounded drugs, which, in turn, will make it less likely that manufacturers will take advantage of the compounding loophole. This argument is based on two assumptions. First, because pharmacists do not need FDA approval in order to sell their compounded drugs, they have an unfair competitive advantage over drug manufacturers. In order to level the playing field and maintain drug manufacturers' incentive to comply with the FDA approval requirements, a market for particular compounded drugs cannot be allowed to develop. Second, if consumers do not know about particular compounded drugs, they will be less likely to ask for them. Manufacturers, in turn, will be less tempted to circumvent the FDCA through compounding if they cannot advertise their "compounded" drugs to stimulate consumer demand.

1. The government's asserted goals can be achieved without infringing on pharmacists' fundamental right to free speech.

The government cannot demonstrate that speech restrictions are necessary to achieve its stated goal of preserving the

[73] The government's argument, however, is apparently more hypothetical than real, since it has not presented evidence demonstrating that drug manufacturers have used pharmacies as "fronts" to manufacture drugs or that a large number of community pharmacies regularly manufacture medications in bulk.

integrity of the FDA approval process. The asserted governmental interest here is to prevent covert drug manufacturing. The government should address that problem directly. The current food and drug laws provide ample room for the FDA to stop large-scale manufacturing and marketing of unapproved drugs, as the government's prior enforcement actions demonstrate.[74] In addition, the other conditions of Section 503A, *e.g.*, limitations on out-of-state shipments, are an attempt to address this goal directly.

The government argues that the speech restrictions are necessary to achieve its goal because advertising and promotion are proxies for manufacturing. But the proxy is far from perfect. Promotion and advertising are not related exclusively to manufactured goods: even companies that provide completely customized products advertise and promote what they can do, including providing specific examples of particular products. The fact that a company manufactures a product may be a good predictor of whether or not it will promote and advertise that product, but the fact that a company advertises and promotes products and services is not a good indicator of whether those products and services are manufactured on a large scale or are customized creations.

2. The speech restrictions are overbroad.

The FDAMA speech restrictions, as the government explains, are intended to prevent unregulated manufacture of drugs under the guise of compounding. But the speech regulations prohibit advertising of *all* compounded drugs – even those compounded by community pharmacists who are clearly uninvolved in covert drug manufacturing. Section 503A's plain language prohibits pharmacists engaged in traditional compounding from advertising any particular compounded drugs or classes of drugs, even though the government does not dispute

---

[74] See, *e.g.*, *Sene X Eleemosynary*, *supra*; *Cedars N. Towers Pharmacy*, *supra*.

that by compounding such drugs the pharmacist is performing an invaluable public health service.

In the government's view, prohibiting advertising of pharmacist-compounded drugs is permissible because advertising is not "necessary" to traditional compounding as performed by community pharmacists.[75] It may be true that advertising and promotion are not critical to the practice, but that does not mean that community pharmacists who offer compounding services have no interest in promoting their services and advertising particular compounded drugs. To the contrary, like other professionals, they have a strong interest in ensuring that the public is aware of the services and products they can provide.[76]

The government asserts (at 40, 43) that generic advertising regarding the availability of compounding services suffices to meet this need. But that is plainly not so. Advertising concerning the availability of a *particular* pharmacist-compounded drug is far more effective in helping consumers and physicians understand how compounding can help them than information about compounding in general. Many people may not understand what "compounding" services are or how they can assist them. Accordingly, an advertisement explaining only that the pharmacist can "compound" drugs will not inform the parent of a child who will not take his medicine that the pharmacist can make the medicine taste like the child's favorite candy. On the other hand, an advertisement for strawberry or peppermint flavored ampicillin would get the message across.

The FDAMA speech restrictions are also overbroad because they do not circumscribe advertising, promotion, and solicitation to the general public alone. Rather, Section 503A prohibits

---

[75] See U.S. Br. 34.

[76] See, *e.g.*, *Bates* v. *State Bar of Arizona*, 433 U.S. 350, 354, 383 (1977) (attorneys); *Virginia State Bd. of Pharmacy*, 425 U.S. at 762 (pharmacists).

all advertising and promotion of compounding services and compounded drugs, including that directed to physicians – a highly educated audience that is capable of understanding and evaluating such information and using it judiciously. When an independent pharmacist and physician discuss medication possibilities, the conversation is between equals. Each may have a particular expertise, but they both are capable of deciphering and understanding sophisticated and complicated medical information. Any concern that physicians will be misled by or unable to understand advertising regarding the compounding of specific drugs is entirely unfounded.

Limiting information to doctors also cannot be justified on the grounds of overreaching or undue influence. The provision of accurate factual information through promotion and advertising does not sway or influence the doctor's choice of therapy. Such is allegedly the case with some marketing tools – *e.g.*, free tickets, meals, or other perks – used by drug companies to sell manufactured drugs to physicians,[77] but there is no hint of that here. Without good reason, Section 503A simply prevents physicians (and their patients) from receiving potentially useful – and even necessary – information regarding alternatives to mass-produced, one-size-fits-all drug products.

[77] This practice has garnered substantial criticism within and without the medical profession, because some believe doctors may be unduly influenced in deciding what drugs to prescribe to their patients. See, *e.g.*, Joseph P. Shapiro & Stacey Schultz, *Prescriptions: How Your Doctor Makes the Choice*, U.S. News & World Rept. 58 (Feb. 19, 2001); Ashley Wazana, *Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift*, 283 J. Am. Med. Assoc. 373-380 (2000); Warren E. Leary, *Doctors Given Millions by Drug Companies*, N.Y. Times B13 (Dec. 12, 1990). Notably, however, the federal government does not prohibit this type of advertising or solicitation.

3. The government's arguments make no sense even on their own terms.

The government's arguments are also wholly unpersuasive even on their own terms. To begin with, there is no evidence that the demand for pharmacist-compounded drugs and pharmacists' compounding services is artificially high – that is, that advertising has led more people to demand pharmacist-compounded drugs than actually require them.

Moreover, the government presumes that compounding pharmacists compete with drug manufacturers in a meaningful sense. This concern is exaggerated, to say the least. Although compounding is important to public health and assists millions of patients, the fact remains that, at the very most, no more than 10 percent of prescriptions nationwide are filled through pharmacist compounding.

Finally, it is unlikely that most drug manufacturers would forgo FDA approval, even if given the chance. As the international "gold standard" for prescription medications, FDA approval opens up access not only to the U.S. market but to markets worldwide.[78] Pharmaceutical companies are unlikely to dispense with the FDA imprimatur, if doing so would mean losing access to these markets as well as valuable reputational and marketing benefits. There is thus no demonstrated need to close the compounding "loophole" in the manner set forth by the FDAMA.

4. The government cannot regulate conduct indirectly by restricting truthful commercial speech.

Government prohibitions on commercial speech contravene the First Amendment when, rather than protect consumers from false or misleading information, they are designed to shield

[78] See, *e.g.*, *U.S. Drugs Speed to Russian Markets*, FDA Consumer 4 (May 1994); Dixie Farley, *FDA's Global Reach to Protect Public Health*, FDA Consumer 6 (Nov. 1986).

consumers from the truth or regulate their or others' conduct indirectly: a governmental interest in keeping consumers "ignorant in order to manipulate their choices in the marketplace" is "per se illegitimate."[79]

In this instance, Congress is restricting pharmacists' speech in an attempt to regulate their and drug manufacturers' conduct indirectly. Paternalism is (apparently) not the motivating factor behind the speech restrictions, but Section 503A nonetheless aims to regulate an industry through consumer ignorance: if consumers are ignorant of pharmacist-compounded drugs, they will likely request only manufactured products, and drug manufacturers will continue to comply with the various FDCA requirements. Given that the government cannot limit information and restrict speech in order to prevent the public from receiving information that is potentially dangerous or harmful, the government certainly cannot restrict speech simply because it has decided it wants to manipulate consumer demand to prop up its regulatory scheme. Rather than impinge on the constitutional rights of pharmacists and consumers, the government should achieve its goals directly by regulating the conduct of those who violate the FDCA.[80]

---

[79] *44 Liquormart*, 517 U.S. at 518 (Thomas, J., concurring in part); see also *id.* at 517 (Scalia, J., concurring in part) (expressing "aversion towards paternalistic governmental policies that prevent men and women from hearing facts that might not be good for them").

[80] See *Central Hudson*, 447 U.S. at 564 (noting "the Court has declined to uphold regulations that only indirectly advance the state interest involved"). For example, advertising bans cannot be imposed to protect the ethical standards of a profession. See, *e.g.*, *Bates*, 433 U.S. at 378 ("Restraints on advertising * * * are an ineffective way of deterring shoddy work."). See also *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 491 (1995) (prohibition against including alcohol content on beer labels was "more extensive than necessary" because government had alternative options to advance its interest "in a manner less intrusive to respondent's First Amendment rights").

That the government's larger goal is to preserve the public's health and welfare does not justify the suppression of valuable information and market regulation through consumer ignorance. This approach was soundly rejected in *Virginia State Bd. of Pharmacy*, the first case to recognize First Amendment protection for commercial speech:

> There is, of course, an alternative to this highly paternalistic approach. That alternative is to assume that this information is not in itself harmful, that people will perceive their own best interests only if they are well enough informed, and that the best means to that end is to open the channels of communication rather than to close them. * * * It is precisely this kind of choice, between the dangers of suppressing information and the dangers of its misuse * * *, that the First Amendment makes for us.[81]

By limiting information, and keeping consumers and physicians in the dark about drugs that can be made available through compounding, Section 503A prevents consumers from learning about and receiving beneficial – or even essential – drug therapies. Causing patients who cannot use mass-produced pharmaceutical products (*e.g.*, because they have allergies, cannot swallow, or cannot keep a medicine down) to be unaware of concrete solutions to their medication needs is a far greater menace to public health and well being than having truthful information regarding these options available in the marketplace.

CONCLUSION

The judgment of the court of appeals should be affirmed.

---

[81] 425 U.S. at 770.

Respectfully submitted.

JOHN M. RECTOR
General Counsel
National Community
Pharmacists Association
205 Daingerfield Road
Alexandria, VA 22314
(703) 683-8200

KENNETH S. GELLER*
BRITTON B. GUERRINA
Mayer, Brown & Platt
1909 K Street, N.W.
Washington, D.C. 20006
(202) 263-3000

* *Counsel of Record*

JANUARY 2002

No. 01-344

Supreme Court, U.S.
FILED
JAN 17 2002
CLERK

In the Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES, ET AL.,

Petitioners,

v.

WESTERN STATES MEDICAL CENTER, ET AL.,

Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Ninth Circuit

BRIEF OF THE INTERNATIONAL ACADEMY OF COMPOUNDING PHARMACISTS AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENTS

JEFFREY N. GIBBS
JENNIFER B. DAVIS
JEFFREY N. WASSERSTEIN
Hyman, Phelps & McNamara, PC
700 Thirteenth Street, N.W.
Suite 1200
Washington, D.C. 20005
(202) 737-5600

ALAN E. UNTEREINER
ARNON D. SIEGEL*
Robbins, Russell, Englert, Orseck & Untereiner LLP
1801 K Street, N.W.
Suite 411
Washington, D.C. 20006
(202) 775-4500

* *Counsel of Record*

BEST AVAILABLE COPY

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES iii

INTEREST OF THE *AMICUS CURIAE* 1

SUMMARY OF ARGUMENT 1

ARGUMENT 2

I. Introduction 2

II. Historical Evidence Belies the Government's Suggestion that Compounding Was Illegal Prior to FDAMA 6

A. Compounding Has Always Been an Accepted Part of the Practice of Pharmacy 6

B. Pharmacists Supported the Passage of the FDCA 7

C. The Legislative History of the FDCA Demonstrates the Acceptance of the Practice of Compounding 9

D. The Actions of the Federal Government and Members of the Pharmacy Profession, As Well As Official Compendia, Make Clear That Compounding Was Not Regulated by the FDCA 11

E. Post-Enactment Historical Evidence Supports the Proposition that Compounding Was Not Governed by the FDCA 14

F. In the Years Immediately Prior to Enactment of FDAMA, Compounding Was Widely Recognized as Legal 17

G. The Legislative History of FDAMA Supports the Proposition that Compounding Was Not Regulated by the FDCA 21

III. This Court's Commercial Speech Doctrine Protects Advertising for Legal Activities Such as Pharmacy Compounding 22

CONCLUSION 24

TABLE OF AUTHORITIES

Page(s)

Cases

Brown & Williamson v. *FDA*, 529 U.S. 120 (2000) 4-5

Cedars North Towers Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978) 5

Central Hudson Gas & Elec. Corp. v. *Public Serv. Comm'n*, 447 U.S. 557 (1980) ..... *passim*

Professionals & Patients for Customized Care v. *Shalala*, 56 F.3d 592 (5th Cir. 1995) 5

United States v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988) 5

United States v. *Algon Chem. Inc.*, 879 F.2d 1154 (3d Cir. 1989) 5

United States v. *Dianovin Pharm., Inc.*, 475 F.2d 100 (1st Cir. 1973) 3

United States v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983) 5

Virginia State Bd. of Pharmacy v. *Virginia Citizens Consumer Council*, 425 U.S. 748 (1976) 22-23

Warner-Lambert Co. v. *Heckler*, 787 F.2d 147 (3d Cir. 1986) 4

TABLE OF AUTHORITIES—Continued

Page(s)

Constitution and Statutes

U.S. CONST. amend. I ..... *passim*

21 U.S.C. § 321(j) 12

21 U.S.C. § 331(d) 4

21 U.S.C. § 333(a) 4

21 U.S.C. § 351(b) 12

21 U.S.C. § 352(g) 12

21 U.S.C. § 353a ..... *passim*

21 U.S.C. § 355(a) 9

21 U.S.C. § 360(b) 16

21 U.S.C. § 360(g)(1) 16

21 U.S.C. § 374(a)(2)(A) 17

21 U.S.C. § 802(15) 17

Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1236 17

Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 ..... 3, 16-17

Federal Food and Drugs Act of 1906, Pub. L. No. 59-384, 34 Stat. 768 ..... 7, 13

TABLE OF AUTHORITIES—Continued

Page(s)

Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 ..... *passim*

Food and Drug Administration Modernization Act of 1997, Pub. L.No. 105-115, 111 Stat. 2296 .... *passim*

Ark. Code Ann. § 17-92-102 9

Mass. Regs. Code tit. 247, § 9.01(16) 20

Minn. R. 6800.2250 20

N.D. Admin. Code § 61-04-04-01(14) 20

Miscellaneous

Abstract of the Proceedings of the House of Delegates, APhA, 17 J. AM. PHARM. ASS'N 1052 (1938) 13

81 CONG. REC. 2001 (1937) 9-10

83 CONG. REC. 2279 (app.) (1938) 10-11

DISPENSING OF MEDICATION (9th ed. 1984) 15-16

Ernest, *Pharmacists in the Civil Service*, 1940 J. AM. PHARM. ASS'N 301 12

Fischelis, *Golden Anniversary Address*, 15 J. AM. PHARM. ASS'N 476 (1936) 7-8

Fischelis, *Federal Drug Legislation Must Not Be Permitted to Die*, 14 J. AM. PHARM. ASS'N 349 (1935) 8

TABLE OF AUTHORITIES—Continued

Page(s)

GUIDANCE FOR INDUSTRY: PROVIDING CLINICAL EVIDENCE OF EFFECTIVENESS FOR HUMAN DRUG AND BIOLOGICAL PRODUCTS (FDA 1998) 4

History and Background Information on USP's Activities in Compounding Pharmacy Practices, 27 PHARMACOPEIAL F. 3169 (2001) 6

HUSA'S PHARMACEUTICAL DISPENSING (6th ed. 1966) ... 15

Joint Session of the American Pharmaceutical Association, the American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy, 17 J. AM. PHARM. ASS'N 1000 (1938) 6, 13

Jurisprudence in the Pharmaceutical Curriculum, 1940 J. AM. PHARM. ASS'N 273 13-14

Klumpp, *The Philosophy of the Food, Drug and Cosmetic Act*, 1941 J. AM. PHARM. ASS'N 379 14

Memorandum for Ass't Sec'y of the Army, Navy & Air Force from Ass't Sec'y of Defense re: Tri-Service Pharmacy Policy Guidance (Jul. 26, 1995), *available at* http://www.tricare.osd.mil/policy/fy95/pharmpol.html 19

NATIONAL ASS'N OF BDS. OF PHARMACY, MODEL STATE PHARMACY ACT 18, 20

National Formulary 12

National Survey of Quality Assurance Activities for Pharmacy-Prepared Sterile Products in Hospitals, 48 AMER. J. OF HOSP. PHARM. 2398 (1991) 21

TABLE OF AUTHORITIES—Continued

Page(s)

O'CONNELL & PETTIT, A MANUAL OF PHARMACEUTICAL LAW (1938) 7

PETTIT, MANUAL OF PHARMACEUTICAL LAW (3d ed. 1962) 14, 16

Pharmaceutical Care: Part of TQM?, DRUG TOPICS 10 (July 10, 1995) 21

Proceedings of the Local Branches, 14 J. AM. PHARM. ASS'N 232 (1935) 6

REMINGTON'S PRACTICE OF PHARMACY (8th ed. 1936) 6, 7

REMINGTON'S PRACTICE OF PHARMACY (10th ed. 1951) 14-15

REMINGTON'S PRACTICE OF PHARMACY (12th ed. 1961) 6, 15

REMINGTON'S PHARMACEUTICAL SCIENCES (14th ed. 1970) 15

S. REP. NO. 105-43 (1997) 19, 21

Schwartz, *Pharmacy in the U.S. Navy*, 1940 J. AM. PHARM. ASS'N 299 12

Smith, *Training Army Pharmacy Technicians*, 1940 J. AM. PHARM. ASS'N 296 11-12

Swain, *Legislative Weather-Vanes*, 15 J. AM. PHARM. ASS'N 794 (1936) 8, 9

THE PHARMACEUTICAL CURRICULUM (1952) 16

TABLE OF AUTHORITIES—Continued

Page(s)

Underhill, *Regulatory and Clinical Aspects of the Resurgence of Compounding by Pharmacists*, 22 DRUG. DEV. & INDUS. PHARMACY 659 (1996) 19

U.S. Pharmacopoeia XII (1942) 12-13

VETERANS HEALTH ADMINISTRATION – PHARMACY SERVICE, VA HANDBOOK 7610 (Jan. 11, 1990), *available at* http://www.va.gov/facmgt/standard/space_idx.asp 19

INTEREST OF THE *AMICUS CURIAE*[1]

Amicus curiae the International Academy of Compounding Pharmacists ("IACP") is an international non-profit association devoted to the protection and advancement of pharmaceutical compounding – one of the essential elements of the profession of pharmacy. The IACP's membership consists of more than 1400 pharmacists who engage in compounding, as well as approximately 200 other members, including physicians, patients, pharmacy students, and retired pharmacists. In defending the constitutionality of the limitations on speech relating to compounding, the government has asserted that the "introduction of compounded new drugs into interstate commerce" (Pet. Br. 18) was "unlawful in all circumstances" prior to 1997. According to the government, compounded drugs have been subject to a "generally applicable prohibition on [their] distribution" (*id.*) and "would be (and [are]) prohibited" (*id.* at 19) unless the statute at issue in this case is upheld. That position, if accepted, would devastate IACP's members in their practice of pharmacy and in their ability to serve patients' needs. The IACP thus has a critical interest in seeing that the Court be given an accurate picture of the law and history of pharmaceutical compounding. Moreover, IACP members regularly advertise. They thus have a strong interest in not being subjected to the unconstitutional limits on their speech imposed by the statute at issue in this case.

SUMMARY OF ARGUMENT

The government's defense of the limits on speech relating to pharmaceutical compounding rests on the suggestion that compounding was illegal from 1938, when the Federal Food, Drug, and Cosmetic Act was enacted, until 1997, when the statute at issue in this case was enacted. The government is simply wrong. Far from being illegal for 59 years, pharmaceuti-

---

[1] Pursuant to this Court's Rule 37.3, letters from the parties consenting to the filing of this brief have been lodged with the Clerk of the Court. Counsel for *amicus curiae* wrote this brief in its entirety. No person or entity, other than the *amicus curiae*, its members, or its counsel, has made a monetary contribution to the preparation or submission of this brief.

cal compounding has long been an essential part of the practice of pharmacy – as ample historical evidence makes clear. Because compounding has always *been* legal, the government can have no interest, much less a substantial one, in saying that it can be *made* legal only if coupled with a restriction on advertising. The limits on speech concerning pharmaceutical compounding are unconstitutional.

ARGUMENT

I. Introduction

Under *Central Hudson Gas & Elec. Corp.* v. *Public Serv. Comm'n*, 447 U.S. 557 (1980), restrictions on commercial speech pass muster under the First Amendment if, and only if, the governmental interests underlying the restriction are "substantial"; the speech limitation "directly advances the governmental interest[s] asserted"; and the regulation is "not more extensive than is necessary to serve [the] interest[s]." *Id.* at 566; see Pet. App. 4a-5a. In arguing that Section 503A of the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 353a,[2] is constitutional, the government says that the statute directly advances several interests "substantial" enough under *Central Hudson*: "preserv[ing] the effectiveness and integrity of the FDCA's new drug approval process" (Pet. Br. 19); "preserv[ing] the availability of compounded drugs" (*id.*); and "[a]chieving the proper balance between these two independently compelling but competing interests" (*id.* at 20).

But *Central Hudson* protects speech concerning only "lawful activity" (447 U.S. at 553), and here the government says that accurate advertising concerning compounded drugs relates to an activity that is "lawful" only because Congress has created a "carefully circumscribed exemption." Pet. Br. 18. In

[2] Section 503A of the Federal Food, Drug, and Cosmetic Act of 1938 ("FDCA"), Pub. L. No. 75-717, 52 Stat. 1040, was added by the Food and Drug Administration Modernization Act of 1997 ("FDAMA") Pub. L. No. 105-115, 111 Stat. 2296.

contrast, the government says, "[b]efore 1997," when FDAMA was signed into law, "the introduction of compounded new drugs into interstate commerce * * * was unlawful in all circumstances." *Id.* This means that but for the speech restrictions at issue in this case compounding "would be (and is) prohibited" (*id.* at 19); see also *id.* at 6 (maintaining that "[i]ntroduction of compounded drugs into interstate commerce without the approval of the FDA was thus illegal before enactment of FDAMA * * * and it remains illegal today unless the requirements in Section [503A] are satisfied") (citation omitted).

The implications of the government's view are breathtaking. The FDA has consistently taken the position that if drug *components* have moved through interstate commerce, the agency has jurisdiction over the product. See, *e.g.*, *United States* v. *Dianovin Pharm., Inc.*, 475 F.2d 100, 102-03 (1st Cir. 1973). At least one component of every compounded drug is invariably shipped in interstate commerce. Thus, under the government's theory, *all* extemporaneously compounded drugs would need to go through the rigorous new drug application ("NDA") process in order to be dispensed. The government's argument – if adopted – would effectively render all compounding without an NDA illegal, even if the product is dispensed intrastate.

But compounded drugs cannot comply with the NDA requirements. As enacted in 1938, the FDCA mandated that the sponsor of a "new drug" submit, among other things, "full reports of investigations which have been made to show whether or not such drug is safe for use." Pub. L. No. 75-717; FDCA § 505(b). (The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (the "1962 Amendments") added the requirement that sponsors of new drugs demonstrate the efficacy of the drug as well.) Extemporaneously compounded drugs are

compounded drugs intended for use in a single patient, but conducting "investigations" with a single patient is impossible.[3]

Even if a pharmacist received several prescriptions for the same compounded drug, she could not possibly conduct clinical studies, submit the NDA, and await FDA approval in time to provide treatment for the patients. Furthermore, as the government notes, a separate FDA approval would be needed any time a physician's prescription called for even the slightest variation in the compounded drug, such as a different dose or route of administration. Pet. Br. 26. The preclusive effect of the NDA requirement is not merely a question of cost, as the government asserts, *id.*, but of the impossibility of conducting clinical studies and allowing the patient to receive promptly the medications prescribed by the physician. Even more astonishing, if the government is right that FDA approval is required for all compounded drugs, then on every occasion since 1938 that a pharmacist extemporaneously compounded a drug for a patient, the pharmacist was acting in violation of the FDCA – a statute that makes it a crime to violate the "new drug" provisions. FDCA § 301(d), 21 U.S.C. § 331(d); see FDCA § 303(a) (providing for imprisonment and/or fines for violations of § 301), 21 U.S.C. § 333(a).

The government, however, is wrong. Contrary to the government's suggestion that compounding was illegal until FDAMA created a limited "exemption" that allowed it, compounding is, and always has been, an essential and lawful part of the practice of pharmacy. In a rewriting of history reminiscent of the position it took in *Brown & Williamson* v. *FDA*, 529

---

[3] FDA has repeatedly interpreted "investigations" to mean more than one clinical trial. In a guidance document drafted pre-FDAMA regarding clinical evidence of effectiveness (a requirement added in 1962), the agency asserted that "Congress generally intended to require at least two adequate and well-controlled studies * * * to establish effectiveness." GUIDANCE FOR INDUSTRY: PROVIDING CLINICAL EVIDENCE OF EFFECTIVENESS FOR HUMAN DRUG AND BIOLOGICAL PRODUCTS 3 (FDA 1998) (citing *Warner-Lambert Co.* v. *Heckler*, 787 F.2d 147 (3d Cir. 1986)).

U.S. 120 (2000), the government is asserting here that Congress banned compounding in the FDCA in 1938, then decided to permit it in FDAMA in 1997 subject to the limits on advertising. In point of fact, only recently did the FDA claim for the first time that agency approval of compounded drugs was required.[4]

As we explain below, the FDCA was not intended to, and did not, give the federal government the authority to regulate, much less ban, the practice of extemporaneous compounding. Rather, like the practice of medicine, regulation of the practice of pharmacy compounding was left by Congress to the states. Considerable historical evidence demonstrates that the FDCA was not intended to halt the practice of compounding; conversely, there is a complete lack of any historical or legislative evidence supporting the position staked out by the government.

---

[4] The district court decisions in *United States* v. *Sene X Eleemosynary Corp.*, 479 F. Supp. 970 (S.D. Fla. 1979), aff'd, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983), and *Cedars North Towers Pharmacy, Inc.* v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978), do not support the government's argument that courts have held that compounding creates "new drugs." Pet. Br. 5-6. Both of these decisions involved "pharmacies" that were engaged in the wholesale manufacture of new drugs rather than drugs that were extemporaneously compounded, for individual patients. The circuit court decisions in *United States* v. *Algon Chem. Inc.*, 879 F.2d 1154 (3d Cir. 1989), and *United States* v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988), are similarly inapposite. Pet. Br. 5-6. Both decisions involved the sale of bulk veterinary drugs, not extemporaneously compounded drugs for individual human patients. Finally, the government's citation of *Professionals & Patients for Customized Care* v. *Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995), for the proposition that compounding creates a "new drug" is incorrect. Pet. Br. 5. The referenced footnote merely notes that the FDCA does not expressly exempt pharmacies or compounded drugs from the new drug, adulteration or misbranding provisions. The legality of compounding was not squarely presented in that case, which involved a challenge to an FDA Compliance Policy Guide on procedural grounds and not the substantive interpretation of the FDCA as applied to compounding. To the extent that the footnote suggests that compounding creates "new drugs" under the FDCA, it is incorrect.

II. Historical Evidence Belies the Government's Suggestion that Compounding Was Illegal Prior to FDAMA

A. *Compounding Has Always Been an Accepted Part of the Practice of Pharmacy*

Remington's Practice of Pharmacy – often described as the "Bible" of pharmacy practice, and relied on widely in colleges of pharmacy both historically and today – stated in 1936 that "[p]harmacy is the science which treats of medicinal substances. It embraces not only a knowledge of medicines and the art of preparing and dispensing them, but also their identification, selection, preservation, combination, analysis and standardization* * *. *Compounding* consists of the skilful blending of two or more ingredients." REMINGTON'S PRACTICE OF PHARMACY 1 (8th ed. 1936) (emphasis in original). Compounding has been part of the practice of pharmacy since its inception. An Egyptian papyrus scroll dating from the 16th century B.C. discussed the compounding of medicines. *Id.* at 3-4. In this country, John Winthrop, Jr. (1606-1676), son of the first governor of Massachusetts, was one of the first Americans to practice pharmaceutical compounding. REMINGTON'S PRACTICE OF PHARMACY 13 (12th ed. 1961). The United States Pharmacopoeia – an official compendium of drug information recognized as authoritative by the FDCA – has included instructions on compounding medications since 1820. *History and Background Information on USP's Activities in Compounding Pharmacy Practices*, 27 PHARMACOPEIAL F. 3169 (2001).

In 1938, when the FDCA was enacted, pharmacy compounding was ubiquitous. Pharmacists compounded more than 250 million prescriptions annually. *Proceedings of the Local Branches*, 14 J. AM. PHARM. ASS'N 232, 233 (1935). In addition, the pharmacy laws of every state defined the practice of pharmacy to include compounding. *Joint Session of the American Pharmaceutical Association, the American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy*, 17 J. AM. PHARM. ASS'N 1000, 1010-13 (1938). For example, New York's pharmacy act defined

"pharmacy" to mean a place in which "drugs, chemicals, medications, prescriptions, or poisons are compounded." REMINGTON'S PRACTICE OF PHARMACY 1352 (8th ed. 1936); see also O'CONNELL & PETTIT, A MANUAL OF PHARMACEUTICAL LAW 159 (1938) (Pennsylvania law defined "pharmacy" similarly). The New Jersey Board of Pharmacy promulgated regulations providing that pharmacy interns were required to compound personally at least 600 prescriptions during their internship in order to be licensed. *Id.* at 23 n.1.

B. *Pharmacists Supported the Passage of the FDCA*

In the years immediately preceding the passage of the FDCA, the American Pharmaceutical Association ("APhA"), the first professional association of pharmacists, strongly supported passage of the FDCA. APhA supported the legislation because of concerns that manufactured proprietary and patent medications were largely unregulated under the Federal Food and Drugs Act of 1906, Pub. L. No. 59-384, 34 Stat. 768. Pharmacists were apprehensive about the quality of manufactured products, as well as the manufacturers' advertising practices. In a 1936 article, Robert P. Fischelis, the President of APhA, remarked:

> We see the actual compounding of medicines taken over by large manufacturing units and the reduction of the average retail pharmacist to a dispenser of ready-made medicines.
>
> Without adequate control over advertising and production of their remedies, the public is being educated by manufacturers to medicate itself, and the use of possibly harmful drugs, without medical or pharmacal [sic] advice, is being encouraged to the point where public health demands some type of supervision. Passage of a revised Federal Food and Drug Law giving the U.S. Food and Drug Administration control over advertising [of manufactured drugs], requiring the disclosure of the formulae of proprietary remedies and strengthening the public control over the drug industry, is

> essential to the public welfare and should be forthcoming at this session of Congress.

Golden Anniversary Address, 15 J. AM. PHARM. ASS'N 476, 476 (1936). In a 1935 editorial, Fischelis wrote:

> It is difficult to understand why [opponents of the FDCA], whose chief interest in food and drug legislation is to block efforts to compel truthful labeling and advertising of foods and drugs and to ease the path of fakers in the food and drug industries, should be in a position to thwart the efforts of earnest legislators and respectable citizens in providing proper control of the manufacture and distribution of drug products.

Federal Drug Legislation Must Not Be Permitted to Die, 14 J. AM. PHARM. ASS'N 349, 349 (1935). From the pharmacists' perspective, passage of the FDCA was necessary to control *manufacturers*.

> It seemed monstrous to us that the retail pharmacist must meet a high educational standard, must satisfy exacting State Board requirements and must subject himself to almost continuous regulation and control, while the manufacturer, even though his products are much more widespread in distribution, is required by law to meet no standard whatsoever. In other words, while exacting requirements were thrown around the man who would compound a prescription for a dozen pills, there was no such restriction surrounding the man who might produce these same pills by the ton.

Swain, *Legislative Weather-Vanes*, 15 J. AM. PHARM. ASS'N 794, 796 (1936).

There is no historical evidence that pharmacists believed that the FDCA encompassed extemporaneous pharmacy compounding. Pharmacists were not alone. There is no contemporaneous evidence that anyone – including the FDA –

thought the FDCA would prohibit pharmacy compounding, one of the basic forms of health care in the United States.

C. *The Legislative History of the FDCA Demonstrates the Acceptance of the Practice of Compounding*

Little was stated in the legislative history of the FDCA about the meaning of section 505(a), 21 U.S.C. § 355(a), which prohibited "new drugs" from being introduced into interstate commerce unless they have been approved by the federal government. However, the legislative history does suggest that section 505 was intended to apply solely to manufacturers of new drugs, and was not designed to affect the actions of physicians and pharmacists in fulfilling their professional responsibilities. In fact, physicians, as well as pharmacists, were permitted to compound medicines as part of their practice: "About the only real privilege granted to pharmacists under the pharmacy laws was that of compounding physicians' prescriptions, and this was no exclusive privilege as the pharmacist shared this right with the physician himself." Swain, *supra,* at 795.[5]

The subject of pharmacists arose in the debate on S. 5, the bill that became the FDCA, prior to the addition of section 505. The discussion did not directly address drug compounding by pharmacists, but centered on a provision which stated that "No drug defined in an official compendium shall be deemed to be adulterated * * * because it differs from the standard of strength, quality, or purity therefor set forth in an official compendium, if its standard of strength, quality, or purity be plainly stated on its label." 81 CONG. REC. 2001, 2014 (1937).

Senator Copeland observed that if a physician in New Jersey wanted to prescribe Fowler's solution of arsenic in the

---

[5] Physicians continue to compound. See, *e.g.*, Ark. Code Ann. § 17-92-102 (authorizing physicians to compound their own prescriptions). Although state legislatures repeatedly enacted laws permitting physician compounding after 1938, under the government's analysis, all physician compounding was also outlawed that year.

standard strength, he simply had to write "Fowler's solution, U.S.P." on the prescription, and he "may depend upon the ethical standards of the pharmacist filling that prescription that when it is filled it will be * * * 'Fowler's solution, U.S.P.'" *Id.* at 2017. Senator Moore responded:

> That may * * * be true enough. He might also write that on his prescription, and he might also tell the druggist how he wishes him to prepare it. However, that does not alter the fact that the bill provides that no drug below the standard represented by the pharmacopoeia and the other standards is adulterated if on the container the adulteration is made manifest.

Id. This exchange exemplified an awareness that physicians relied on pharmacists to "prepare," *i.e.*, compound, drugs for their patients in accordance with instructions set forth in prescriptions. Such preparation included the compounding of drugs.

That section 505 was targeted toward drug manufacturers, and not physicians and pharmacists, is emphasized in remarks by Representative Coffee which appeared in the June 1, 1938 *Congressional Record*. Representative Coffee argued that S. 5 offered inadequate protection against the type of tragedy that had occurred with the marketing of a new and untested drug, elixir of sulfanilamide, in 1937. 83 CONG. REC. 2279 (app.) (1938). He commented that at the time of the tragedy, Secretary of Agriculture Henry Wallace "made excellent recommendations as to the minimum requirements of legislation which should be enacted to prevent the public thus becoming prey of *criminally careless or ignorant manufacturers*." *Id.* (emphasis added).

In Representative Coffee's view, the proposed section 505, which required the "licensing" of new drugs, failed to incorporate all the provisions believed by Secretary Wallace to be essential. Summarizing Secretary Wallace's and his own concerns, Representative Coffee said:

> Secretary Wallace stated the case for licensing the manufacturers of potentially harmful drugs briefly and well: "In the interest of safety, society had required *that physicians be licensed to practice the healing art. Pharmacists are licensed to compound and dispense drugs*. Electricians, plumbers, and steam engineers pursue their respective trades under license. But there is no such control *to prevent incompetent drug manufacturers from marketing any kind of lethal poison*."

Id. (emphases added). Thus, section 505 of the FDCA was not intended to affect the professional activities of physicians or pharmacists, including their practice of compounding, but to control drug manufacturers. There is no indication whatsoever that Congress intended to ban compounding, which played an irreplaceable role in the health care system. If compounding had been banned in 1938, as the government argues more than sixty years later, the results would have been catastrophic, since there were, in many cases, no alternatives to compounded medications. In 1938, the practice of medicine without compounding was inconceivable.

D. *The Actions of the Federal Government and Members of the Pharmacy Profession, As Well As Official Compendia, Make Clear That Compounding Was Not Regulated by the FDCA*

Considerable historical evidence from the period immediately following the enactment of the FDCA rebuts the government's contention that the statute banned extemporaneous compounding by pharmacists. For example, in a series of articles by United States military and civil service pharmacists, the federal government recognized the importance of compounding as part of the practice of pharmacy in the armed forces and the civil service. See Smith, *Training Army Pharmacy Technicians*, 1940 J. AM. PHARM. ASS'N 296, 297 ("The pharmacy technician has five chief functions * * * (3) routine dispensing and compounding of medications for wards and clinics of the hospital; (4) compounding of prescriptions for

hospital and out-patients * * * ."); Schwartz, *Pharmacy in the U.S. Navy*, 1940 J. AM. PHARM. ASS'N 299, 299 ("Every naval unit to which a medical officer is attached has a fully equipped pharmacy. It has * * * all the paraphernalia required in compounding and dispensing medicine."); Ernest, *Pharmacists in the Civil Service*, 1940 J. AM. PHARM. ASS'N 301, 301 ("Where drugs or medicines are dispensed or doctors' prescriptions are compounded, a duly qualified registered pharmacist is found to be employed."). There is no indication in these discussions that compounding results in a new drug that must be approved by FDA, or that federal employees were being advised to break the law. Rather, compounding is discussed in the articles by federal government officials as an accepted part of the practice of pharmacy, rather than, as now asserted by the government, a crime.

Moreover, both the United States Pharmacopoeia ("USP") and the National Formulary ("NF") recognized the practice of compounding and included instructions for compounding numerous drugs as part of their compendial standards. See, *e.g.*, U.S.P. XII, at 364-65 (1942) (instructions for compounding pills of ferrous carbonate); *id.* at 446-48 (suppositories); *id.* at 505-06 (tinctures); *id.* at 532-41 (ointments); N.F. VII, at 400-01 (1942) (syrups); *id.* at 439-40 (tinctures); *id.* at 469-77 (ointments).

The inclusion of compounding formulas in the USP and NF is strong evidence that compounding was widely recognized as legal. Congress identified both the USP and NF as "official compendia" in the FDCA. FDCA § 201(j); 21 U.S.C. § 321(j). Any product or compounded preparation listed in a monograph in the USP or the NF must therefore comply with the compendial standards or they are deemed adulterated and misbranded. FDCA §§ 501(b) (adulteration), 502(g) (misbranding), 21 U.S.C. §§ 351(b), 352(g). These compendia are the only statutorily recognized compendia in the FDCA. Indeed, the importance of the USP was such that numerous federal government health officials, including representatives from the FDA, the medical departments of the Army and Navy, the U.S. Public

Health Service, and the Department of Commerce, were delegates to the U.S. Pharmacopeial Convention of 1940. U.S.P. XII, at lix. Just two years after the enactment of the FDCA, this USP Convention adopted monographs for many compounded drugs.

Similarly, the pharmacy profession clearly understood that the FDCA did not ban compounding. First, APhA celebrated the enactment of the FDCA, stating in a 1938 article that:

> It is gratifying to be able to note the enactment of the new Food, Drug and Cosmetic Legislation by the Federal government, to supplant the outmoded statute of 1906 * * * . We believe, despite the opposition encountered, that a greatly improved piece of legislation has been enacted, and that it is going to bring about a more wholesome condition in the field of manufactured medicinal products.

Abstract of the Proceedings of the House of Delegates, APhA, 17 J. AM. PHARM. ASS'N 1052, 1055 (1938). Second, following the passage of the FDCA, APhA supported state pharmacy legislation to complement the federal act. APhA proposed model legislation that stated that the "term 'pharmacy' * * * shall be held to mean and include every store or shop or other place * * * where physicians' prescriptions are compounded * * * ." *Joint Session of the American Pharmaceutical Association*, *supra*, 17 J. AM. PHARM. ASS'N at 1013. Under the government's novel theory, this legislation defined pharmacy in terms of an illegal act. Further, in an article entitled *Jurisprudence in the Pharmaceutical Curriculum*, an officer of the APhA noted that:

> Everyone with any familiarity at all with the field knows that, while *the Federal Food, Drug and Cosmetic Act has only an indirect relation to the pharmacist engaged in the operation of a retail drug store* within a given area of any given state, also knows that this same pharmacist is held to a strict observance of another federal law; namely, the Harrison Narcotic Act [predecessor to the Controlled

> Substances Act, see *infra* at 17.]. The mere fact that one act of Congress imposes a heavy burden upon the pharmacist, *while another Congressional act is only of incidental importance to him*, should, at least, stimulate his curiosity.

1940 J. AM. PHARM. ASS'N 273, 273 (emphases added).

Just as there is no evidence that pharmacists believed that one of their primary functions had been outlawed by the FDCA, there is no evidence that FDA ever asserted that the FDCA regulated compounded drugs as new drugs. Indeed, in an article in the *APhA Journal* addressed to pharmacists, a former senior FDA drug official discussed the "new drug" provision of the FDCA without any mention that it affected the practice of compounding. See Klumpp, *The Philosophy of the Food, Drug and Cosmetic Act*, 1941 J. AM. PHARM. ASS'N 379, 381 (written by the former Chief of the Drug Division of the FDA).

E. *Post-Enactment Historical Evidence Supports the Proposition that Compounding Was Not Governed by the FDCA*

The historical evidence from the years that followed the enactment of the FDCA demonstrates that compounding remained an integral part of health care. No one asserted that compounding was made illegal by the FDCA, while every state affirmatively authorized the compounding of drugs. "In mentioning rights of pharmacists, state statutes generally list the following as rights: to practice pharmacy, * * * to compound prescriptions * * * ." PETTIT, MANUAL OF PHARMACEUTICAL LAW 26 (3d ed. 1962). The 1951 edition of *Remington's Practice of Pharmacy* included a discussion of the FDCA without any mention of compounding being regulated under the Act. It also noted that compounding was both permitted and regulated by the states. REMINGTON'S PRACTICE OF PHARMACY 1163 (10th ed. 1951) ("The practice of pharmacy * * * is regulated by law in every state. The police power, in the basic governmental sense, is invoked to surround the compounding and dispensing of prescriptions."); *id.* at 1173-77 (discussion of FDCA, no mention of compounding); *id.* at 1195-97 (discussion

of minimum equipment needed for compounding and prescription department); *id.* at 1220 (discussion of the prescription, noting that the inscription section of the prescription "contains the names and quantities of the ingredients" used to compound); *id.* at 1227-28 (discussion of the filling and compounding of the prescription); see also REMINGTON'S PRACTICE OF PHARMACY 1567 (12th ed. 1961) (inscription of prescription contains "names and quantities of the prescribed ingredients"); *id.* at 1571 (discussion of the compounding of the prescription); *id.* at 1697 (stating that "[t]he regulation of the practice of pharmacy is a function of the states, and not of the Federal Government"); *id.* at 1706-10 (analysis of FDCA, no mention of compounding). A later edition of *Remington's* made the same point quite plainly: "The regulation of the practice of pharmacy is a function of the states, and not of the Federal Government." REMINGTON'S PHARMACEUTICAL SCIENCES 1963 (14th ed. 1970); see *id.* at 1976-85 (treatment of FDCA, no mention of compounding).

Other pharmacy texts similarly referred to drug compounding as a universally accepted practice regulated by the states. For example, the preface to *Husa's Pharmaceutical Dispensing* – another important pharmacy treatise dealing almost exclusively with compounding – states that "[c]ompounding of medicinal products will always be an important function of the pharmacist in spite of the fact that practically all prescriptions now call for prefabricated medication." HUSA'S PHARMACEUTICAL DISPENSING 36-42 (6th ed. 1966) (discussion of federal and state laws regarding pharmacy; noting that regulation of practice of pharmacy, including "licensure and standards for compounding and dispensing of prescriptions, is embodied in the laws of the various states"). More recent pharmaceutical texts have also discussed the importance of compounding, without noting any federal regulation of the practice. See DISPENSING OF MEDICATION ch. 12 (9th ed. 1984) (chapter on extemporaneously compounded formulations). The authors of the chapter entitled "Extemporaneous formulations" stated that "[t]he purpose of prescription compounding is to dispense safe, effective medication pursuant to the order of a duly licensed practitioner whose

judgment has dictated that individualized drug therapy is required for a patient." *Id.* at 258. The premise underlying this book is that compounding is legal.

While the authors of these widely utilized pharmacy texts clearly understood the importance of the FDCA in regulating the manufacture of drugs, no author even suggested that the FDCA rendered compounded drugs illegal unless approved by the federal government. Indeed, the various treatises from the period are uniform in recognizing that *state* governments – through the state legislatures and state boards of pharmacy – both permitted and regulated compounding.

The government's theory is further belied by the fact that pharmacy students took classes in compounding. For example, a report prepared by the American Association of Colleges of Pharmacy discussed the importance of pharmaceutical compounding as part of the pharmaceutical curriculum. See THE PHARMACEUTICAL CURRICULUM 144-45, 148-49 (1952) (discussing the centrality of compounding courses in colleges of pharmacy). Many states also required practical experience in compounding and dispensing prescriptions prior to licensure. PETTIT, MANUAL OF PHARMACEUTICAL LAW 25-26 (3d ed. 1962). For example, the California Board of Pharmacy required 950 hours of practical experience in the compounding and dispensing of prescriptions. *Id.* at 26. The government's novel contention is that colleges of pharmacy throughout the country were teaching their students about an illegal practice, and that the states were requiring pharmacists to display proficiency in an illegal act to be licensed.

The 1962 Amendments further demonstrate that extemporaneous compounding by pharmacists was not precluded by the FDCA. The 1962 Amendments added provisions to the FDCA, among other things, requiring manufacturers to register with the FDA and list their drugs. See FDCA § 510(b), 21 U.S.C. § 360(b). Pharmacies were (and still are) exempt from these requirements. See FDCA § 510(g)(1) (exempting pharmacies from registration and listing), 21 U.S.C. § 360(g)(1). Pharmacies

were also subject to more limited inspections than manufacturers. FDCA § 704(a)(2)(A), 21 U.S.C. § 374(a)(2)(A). It would make no sense to exempt pharmacies from the relatively trivial paperwork requirements of filing registration and listing forms, were it necessary to comply with the onerous requirements of demonstrating safety and effectiveness of each compounded drug in an NDA. The government's illogical theory is that the 1962 Amendments required pharmacists to prove efficacy through controlled clinical studies for every compounded drug, an impossible task for a drug administered to a single patient, but were exempt from the ministerial task of filing a one-page form to list the drug.

Additional evidence that Congress did not intend the FDCA to govern pharmacy compounding is found in the Comprehensive Drug Abuse Prevention and Control Act of 1970, Pub. L. No. 91-513, 84 Stat. 1236 ("CSA"). In the CSA, Congress defined the term "manufacture" to exclude:

> the preparation, compounding, packaging, or labeling of a drug or other substance in conformity with applicable State or local law by a practitioner as an incident to his administration or dispensing of such drug or substance in the course of his professional practice.

CSA § 102(14), 21 U.S.C. § 802(15). Although there is little discussion of this exemption in the legislative history, it is implausible that Congress would have exempted compounding from regulation under the CSA if the act of compounding without an NDA were illegal under the FDCA. On the contrary, the only explanation is that Congress, in permitting the compounding of controlled substances, did not believe that the FDCA had already banned extemporaneous compounding.

F. *In the Years Immediately Prior to Enactment of FDAMA, Compounding Was Widely Recognized as Legal*

In the years prior to the enactment of FDAMA, two prominent organizations – both of which were given a role by Congress in the regulation of compounding – adopted standards

regulating compounding. By establishing standards for compounding, these organizations both affirmed the legality of compounding. In 1993, the National Association of Boards of Pharmacy ("NABP") – the professional organization whose members are the state boards of pharmacy – adopted Good Compounding Practices as part of their Model State Pharmacy Act. See NABP MODEL STATE PHARMACY ACT app. C.1 (Good Compounding Practices Applicable to State Licensed Pharmacies). These guidelines, adopted in whole or in part by numerous states, set forth minimum standards for the practice of compounding. The standards include detailed instructions regarding equipment, adequate space for compounding, the training and qualifications of personnel involved in compounding, storage of raw materials, and drug compounding controls. In 1996, USP – one of the two official compendia mentioned in the FDCA – stated that "[c]ompounding is an integral part of pharmacy practice and is essential to the provision of health care." USP/NF Supplements 3531 (1996). At that time, USP adopted a monograph setting forth standards for compounding. See *id.* (Chapter <1161> Pharmacy Compounding Practices). The monograph includes standards regarding equipment, facilities, ingredient sources, stability criteria, acceptable compounded dosage forms, record retention, and quality control. Neither the NABP's Good Compounding Practices nor the USP's monograph states that NDAs are required for compounded drugs.

Thus, the two standard-setting organizations identified by Congress in section 503A of FDAMA, 21 U.S.C. § 353a, established compounding guidelines before 503A was enacted. These actions further controvert the government's claim that prior to FDAMA, all compounding resulted in the creation of an illegal new drug.[6]

---

[6] Significantly, both USP and NABP were given roles to play regarding compounding under FDAMA. Congress directed the Secretary of Health and Human Services to consult with NABP in developing a memorandum of understanding for use with the states in regulating the interstate distribution of compounded drugs. FDCA § 503A(b)(3)(B), 21 U.S.C. § 353a(b)(3)(B).

At the same time these standards were developed, even agencies of the federal government continued to promote the practice of compounding. For example, the Department of Defense stated in its policy on pharmacies at military treatment facilities that "[t]he pharmacy may bulk compound pharmaceutical preparations using formulas from official compendiums, other references, or a locally developed formula." Memorandum for Ass't Secretaries of the Army, Navy & Air Force from Ass't Sec'y of Defense re: Tri-Service Pharmacy Policy Guidance (Jul. 26, 1995), *available at* http://www.tricare.osd.mil/policy/fy95/pharmpol.html. The Veterans Health Administration ("VHA") similarly required all VHA pharmacies to set aside sufficient space for extemporaneous compounding. VETERANS HEALTH ADMINISTRATION – PHARMACY SERVICE, VA HANDBOOK 7610, ch. 268, at 268-4 (Jan. 11, 1990), *available at* http://www.va.gov/facmgt/ standard/space_idx.asp.

Moreover, in the years leading up to FDAMA, state legislatures continued to authorize compounding. Congress recognized this fact in the legislative history to FDAMA, stating that "[a]ll States include[d] compounding as a core component of the profession of pharmacy." S. REP. NO. 105-43, at 67 (1997); see also Underhill, *Regulatory and Clinical Aspects of the Resurgence of Compounding by Pharmacists*, 22 DRUG. DEV. & INDUS. PHARMACY 659, 660 (1996) ("Traditionally, compounding by pharmacists of a prescription * * * for a patient has been under the control of the relevant State Board of Pharmacy and in fact 41 of the 50 state laws which define the practice of pharmacy specifically including [sic] 'compounding' per se in their definition"). The government's assertion about the illegality of compounding would nullify the pharmacy laws of all 50 states, for each state explicitly authorized compounding. Indeed, not only did all state legislatures authorize pharmacy compounding, but several state boards of pharmacy also defined

---

Representatives from NABP and USP were to participate in an advisory committee prior to the issuance of regulations implementing section 503A. FDCA § 503A(d), 21 U.S.C. § 353a(d).

"unprofessional conduct of a pharmacist" to include refusing to compound prescriptions.[7] Refusing to compound prescriptions can therefore result in professional discipline by states that require pharmacists to compound.

In the years preceding the enactment of FDAMA, compounding pharmacies differed to an extent in their practices. Most pharmacies engaged in limited extemporaneous compounding to meet the needs of local patients. Other pharmacies began to specialize, and fill prescriptions from a more geographically diverse area. With the growing importance of intravenous admixtures, hospital pharmacies performed increasing amounts of compounding. Regardless of their setting or the geographic area served by these pharmacies, they shared common traits: licensure by state boards of pharmacy, compounding prescriptions pursuant to state legislation explicitly authorizing the practice, and dispensing medications to their patients to fill prescriptions by physicians. They also shared another trait – under the government's contention, all of their compounding was illegal.

Immediately preceding the enactment of FDAMA, standard-setting organizations, federal government agencies and the state boards of pharmacy all permitted compounding when performed in compliance with state regulation. Under the government's revisionist approach, the Department of Defense, the Veterans Health Administration, the state legislatures, the state boards of pharmacy, the U.S. Pharmacopoeia, and the National Association of Boards of Pharmacy were all advocating that pharmacists commit criminal acts.

---

[7] Mass. Regs. Code tit. 247, § 9.01(16); N.D. Admin. Code § 61-04-04-01(14); Minn. R. 6800.2250; see also NABP MODEL STATE PHARMACY ACT, MODEL RULES FOR PHARMACEUTICAL CARE § 5(2) ("Unprofessional conduct shall include * * * [u]nreasonably refusing to Compound or Dispense Prescription Drug Orders that may be expected to be Compounded or Dispensed in Pharmacies by Pharmacists.").

In sum, the government's claim that compounding was illegal prior to the enactment of FDAMA turns history on its head. Between 1938 and 1997, pharmacists dispensed billions of compounded. In 1995, pharmacists compounded approximately 220 million prescriptions. *Pharmaceutical Care: Part of TQM?*, DRUG TOPICS 10 (July 10, 1995). Over 96% of hospitals surveyed by the American Society of Hospital Pharmacists in 1991 engaged in extemporaneous compounding of sterile drug products. *National Survey of Quality Assurance Activities for Pharmacy-Prepared Sterile Products in Hospitals*, 48 AMER. J. OF HOSP. PHARM. 2398, 2401 (1991). Under the government's theory, each drug that was dispensed represented a criminal act. Because compounded prescription drugs cannot be dispensed without a prescription, each of these violations was facilitated by a physician or other authorized prescriber. Aiding and abetting these innumerable violations were the colleges of pharmacy that taught the practice of compounding, the state legislatures that authorized compounding, the state boards of pharmacy that regulated compounding and required pharmacists to maintain compounding equipment, the National Association of Boards of Pharmacy and the USP and other compendia that set forth compounding standards and compounding instructions. Contrary to the government's assertion, Pet. Br. 25, these activities did not occur because Congress had prohibited compounding in 1938 but FDA had silently exercised its enforcement discretion. Rather, they occurred because Congress, in enacting the FDCA, did not outlaw extemporaneous compounding.

G. *The Legislative History of FDAMA Supports the Proposition that Compounding Was Not Regulated by the FDCA*

The legislative history of FDAMA itself shows Congress recognized that compounding was a state-authorized and regulated activity. A Senate Committee Report confirms that "[s]tates currently have the authority to license pharmacists and regulate pharmacies, including the scope of pharmacy practice. All States include compounding as a core component of the profession of pharmacy." S. REP. NO. 105-43, at 67. The fact

that Congress itself recognized that compounding was defined by the states as a "core component" of the practice of pharmacy further demonstrates that compounding was not banned by the FDCA as the government asserts.

III. This Court's Commercial Speech Doctrine Protects Advertising for Legal Activities Such as Pharmacy Compounding

In light of the overwhelming evidence demonstrating that compounding has been legal all along, and not just since the passage of FDAMA, the ban on advertising contained in Section 503A cannot possibly satisfy *Central Hudson*, 447 U.S. at 566.

The government asserts that the limits on speech are needed to "preserve the effectiveness and integrity of the FDCA's new drug approval process." Pet. Br. 19; see *id.* at 33, 37-38. The government posits that compounding pharmacies evade the onerous NDA requirements of section 505(a) of the FDCA, while engaging in the advertisement of new drugs and that this is inequitable to manufacturers, which must comply with section 505(a). The government further speculates that this may encourage others to evade the new drug requirements through compounding rather than filing an NDA.

But compounded drugs are *not subject* to the NDA process and never have been. Compounding pharmacies are not, therefore, evading the requirements of the FDCA (or encouraging others to do so by example), and a ban on advertising compounded drugs cannot "directly advance," or advance at all, the government's interest in NDAs.

The government further argues that Section 503A is necessary lest physicians, spurred by compounding pharmacies' advertisements, otherwise prescribe vast quantities of compounded drugs, rather than commercially available pharmaceutical products. The Court has previously rejected similar arguments. In *Virginia State Bd. of Pharmacy* v. *Virginia Citizens Consumer Council*, 425 U.S. 748, 767 n.21 (1976), the Court rejected arguments that advertisements of low drug prices could

lead to overconsumption, stating that "[b]y definition, the drugs at issue here may be sold only on a physician's prescription. We do not assume * * * that simply because low prices will be freely advertised, physicians will overprescribe, or that pharmacists will ignore the prescription requirement." Likewise, alerting physicians to the availability of specific compounded products will not lead to overprescribing by physicians since the compounded drug will be prescribed only where a medical need exists. The government's argument that the advertising restriction is necessary to preserve a "careful balance" between making compounded drugs available and preventing too much compounding is not directly advanced by the advertising restrictions at issue.

Contrary to the government's arguments, there is considerable value to allowing compounding pharmacies to inform the public about which products they can compound. Many pharmacies specialize in compounding certain types of products, such as respiratory drugs or hormone replacement therapy, yet under FDAMA, pharmacists are not even allowed to advertise the class of drugs that they can compound. If a pharmacist cannot inform a physician of the types of drugs that he is capable of compounding, the physician will not be aware of what options may be available. While manufactured drugs are usually appropriate today, they do not always meet a patient's needs. Compounding is particularly useful for patients who are allergic to dyes, flavors or other excipients. Additionally, compounding is often used to create pain medications for patients who cannot swallow pills, or for patients for whom the standard dosage forms are inappropriate.[8] According to the government, the only appropriate advertisement under FDAMA is that a pharmacy is capable of compounding. This bare assertion of capability does not inform the physician of the types of drugs that a pharmacy can tailor to meet an individual patient's needs pursuant to a physician's instructions.

---

[8] *Amicus Curiae* American Pharmaceutical Association discusses this issue at length.

CONCLUSION

The judgment of the court of appeals should be affirmed.

Respectfully submitted.

JEFFREY N. GIBBS
JENNIFER B. DAVIS
JEFFREY N. WASSERSTEIN
Hyman, Phelps & McNamara, PC
700 Thirteenth Street, N.W.
Suite 1200
Washington, D.C. 20005
(202) 737-5600

ALAN E. UNTEREINER
ARNON D. SIEGEL*
Robbins, Russell, Englert,
Orseck & Untereiner LLP
1801 K Street, N.W.
Suite 411
Washington, D.C. 20006
(202) 775-4500

* *Counsel of Record*

JANUARY 2002